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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS	5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS	6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	7	AUG 27	USPATOLD now available on STN
NEWS	8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	10	SEP 13	FORIS renamed to SOFIS
NEWS	11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS	13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS	14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS	16	OCT 19	BEILSTEIN updated with new compounds
NEWS	17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	18	NOV 19	WPIX enhanced with XML display format
NEWS	19	NOV 30	ICSD reloaded with enhancements
NEWS	20	DEC 04	LINPADOCDB now available on STN
NEWS	21	DEC 14	BEILSTEIN pricing structure to change
NEWS	22	DEC 17	USPATOLD added to additional database clusters
NEWS	23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS	24	DEC 17	DGENE now includes more than 10 million sequences
NEWS	25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS	26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS	27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS	28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS	29	JAN 02	STN pricing information for 2008 now available
NEWS	30	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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=> file registry
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

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STRUCTURE FILE UPDATES:   22 JAN 2008  HIGHEST RN 1000503-75-2
DICTIONARY FILE UPDATES:  22 JAN 2008  HIGHEST RN 1000503-75-2

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=> s vardenafil
L1           4 VARDENAFIL

=> file caplus
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       5.61       5.82

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FILE COVERS 1907 - 23 Jan 2008 VOL 148 ISS 4
FILE LAST UPDATED: 22 Jan 2008 (20080122/ED)

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http://www.cas.org/infopolicy.html

=> s l1 and (hypertension or blood pressure)
<------User Break------>

SEARCH ENDED BY USER

=> s l1
L2 438 L1

=> s l2 and (hypertension or blood pressure)
92325 HYPERTENSION
106 HYPERTENSIONS
92346 HYPERTENSION
(HYPERTENSION OR HYPERTENSIONS)
<------User Break------>

SEARCH ENDED BY USER

=> s l2 and hypertension
92325 HYPERTENSION
106 HYPERTENSIONS
92346 HYPERTENSION
(HYPERTENSION OR HYPERTENSIONS)
L3 70 L2 AND HYPERTENSION

=> s l3 and portal
18470 PORTAL
380 PORTALS
18765 PORTAL
(PORTAL OR PORTALS)
L4 4 L3 AND PORTAL

=> d l4 ibib abs 1-4

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1123280 CAPLUS
DOCUMENT NUMBER: 145:449221
TITLE: Roflumilast and roflumilast N-oxide for the treatment of pulmonary hypertension, and combinations with phosphodiesterase 5 inhibitors
INVENTOR(S): Beume, Rolf; Hatzelmann, Armin; Marx, Degenhard; Schudt, Christian; Tenor, Hermann; Eddahibi, Saadia; Adnot, Serge
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 40pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006111495	A1	20061026	WO 2006-EP61557	20060412
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006237300	A1	20061026	AU 2006-237300	20060412
CA 2604295	A1	20061026	CA 2006-2604295	20060412
EP 1874309	A1	20080109	EP 2006-725734	20060412
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
IN 2007MN01889	A	20071207	IN 2007-MN1889	20071112
KR 2008002950	A	20080104	KR 2007-726282	20071112

PRIORITY APPLN. INFO.:	EP 2005-103147	A	20050419
	WO 2006-EP61557	W	20060412

AB The invention discloses the use of roflumilast, roflumilast-N-Oxide, or a pharmaceutically acceptable salt of either for the treatment of pulmonary hypertension. The invention addnl. discloses the use of roflumilast, roflumilast-N-oxide or a pharmaceutically acceptable salt of either in combination with a phosphodiesterase 5 inhibitor, or a pharmaceutically acceptable salt thereof, for the treatment of pulmonary hypertension.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:149404 CAPLUS
DOCUMENT NUMBER: 144:205821
TITLE: 2-Phenyl-substituted imidazotriazinone derivative phosphodiesterase 5 inhibitors for the treatment of symptoms treatable by increasing cGMP levels
INVENTOR(S): Haning, Helmut
PATENT ASSIGNEE(S): Bayer Healthcare A.-G., Germany
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006015715	A1	20060216	WO 2005-EP8057	20050723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,				

SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

DE 102004038328	A1	20060316	DE 2004-102004038328	20040806
AU 2005270446	A1	20060216	AU 2005-270446	20050723
CA 2575907	A1	20060216	CA 2005-2575907	20050723
EP 1776120	A1	20070425	EP 2005-764196	20050723
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				
CN 101035539	A	20070912	CN 2005-80034023	20050723
IN 2007DN01126	A	20070427	IN 2007-DN1126	20070212
KR 2007041613	A	20070418	KR 2007-705245	20070305
NO 2007001231	A	20070503	NO 2007-1231	20070306
US 2007299088	A1	20071227	US 2007-659624	20070905
PRIORITY APPLN. INFO.:			DE 2004-102004038328A	20040806
			WO 2005-EP8057 W	20050723

OTHER SOURCE(S): MARPAT 144:205821

AB The invention relates to the use of PDE 5 inhibitors, and especially of known 2-phenyl-substituted imidazotriazinone derivs., for producing medicaments for the treatment of symptoms that can be treated by increasing cGMP levels in certain tissues, e.g. acute myocardial infarction and damage caused by reperfusion, various symptoms in the female and male reproductive system and urogenital tract, gastrointestinal diseases, damage caused by diabetes, and liver failure.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:1080763 CAPLUS
DOCUMENT NUMBER: 142:16820
TITLE: Use of a phosphodiesterase V inhibitor for the prophylaxis and/or treatment of portal hypertension
INVENTOR(S): Kreisel, Wolfgang
PATENT ASSIGNEE(S): Universitatsklinikum Freiburg, Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108062	A2	20041216	WO 2004-EP6014	20040603
WO 2004108062	A3	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10325813	A1	20050105	DE 2003-10325813	20030606

DE 10325813 B4 20071220
EP 1635838 A2 20060322 EP 2004-739573 20040603
EP 1635838 B1 20070502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
CN 1871010 A 20061129 CN 2004-80022512 20040603
JP 2006527177 T 20061130 JP 2006-508268 20040603
AT 361074 T 20070515 AT 2004-739573 20040603
ES 2287740 T3 20071216 ES 2004-4739573 20040603
US 2007004744 A1 20070104 US 2006-559694 20060501
PRIORITY APPLN. INFO.: DE 2003-10325813 A 20030606
WO 2004-EP6014 W 20040603

AB The invention discloses a medicament for the prophylaxis and/or treatment of diseases or complications associated with portal hypertension, especially hemorrhagic complications. The invention uses a phosphodiesterase V inhibitor, e.g. sildenafil.

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:590998 CAPLUS
DOCUMENT NUMBER: 139:128037
TITLE: Use of acetylcholine esterase antagonists to treat insulin resistance
INVENTOR(S): Lautt, Wayne W.
PATENT ASSIGNEE(S): Diamedica Inc., Can.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 2003061648 A1 20030731 WO 2003-CA78 20030127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003235609 A1 20031225 US 2003-350478 20030124
CA 2514088 A1 20030731 CA 2003-2514088 20030127
EP 1471905 A1 20041103 EP 2003-700275 20030127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2005519906 T 20050707 JP 2003-561592 20030127
US 2005049293 A1 20050303 US 2004-502066 20041027
PRIORITY APPLN. INFO.: US 2002-350958P P 20020125
WO 2003-CA78 W 20030127

AB A method is provided for reducing insulin resistance in a mammalian subject, comprising administering a suitable acetylcholine esterase antagonist.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS SINCE FILE TOTAL

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                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   19.24      25.06

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)       SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -3.20      -3.20

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=> s ("pde 5" or "pde-5" or phosphdiesterase type 5 or phosphodiesterase five or
"phosphodiesterase-5 or vardenafil) and (hypertension or blood pressure)
MISMATCHED QUOTE 'OR "PHOSPHODIE'
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> s ("pde 5" or "pde-5" or phosphdiesterase type 5 or phosphodiesterase five or
"phosphodiesterase-5" or vardenafil) and (hypertension or blood pressure)
   1 FILES SEARCHED...
L5        1365 ("PDE 5" OR "PDE-5" OR PHOSPHDIESTERASE TYPE 5 OR PHOSPHODIESTER
               ASE FIVE OR "PHOSPHODIESTERASE-5" OR VARDENAFIL) AND (HYPERTENSI
               ON OR BLOOD PRESSURE)

=> l5 and portal
L5 IS NOT A RECOGNIZED COMMAND
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For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

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L6          40 L5 AND PORTAL

=> s l6 and py<=2004
   2 FILES SEARCHED...
L7          10 L6 AND PY<=2004

=> duplicate rem
ENTER L# LIST OR (END):l7
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS, EMBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L7
L8           10 DUPLICATE REM L7 (0 DUPLICATES REMOVED)

=> d l8 ibib abs 1-10

L8   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2004:1080763  CAPLUS
DOCUMENT NUMBER:         142:16820
TITLE:                   Use of a phosphodiesterase V inhibitor for the
                         prophylaxis and/or treatment of portal
                         hypertension
```

INVENTOR(S): Kreisel, Wolfgang
PATENT ASSIGNEE(S): Universitatsklinikum Freiburg, Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108062	A2	20041216	WO 2004-EP6014	20040603 <--
WO 2004108062	A3	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10325813	A1	20050105	DE 2003-10325813	20030606
DE 10325813	B4	20071220		
EP 1635838	A2	20060322	EP 2004-739573	20040603
EP 1635838	B1	20070502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1871010	A	20061129	CN 2004-80022512	20040603
JP 2006527177	T	20061130	JP 2006-508268	20040603
AT 361074	T	20070515	AT 2004-739573	20040603
ES 2287740	T3	20071216	ES 2004-4739573	20040603
US 2007004744	A1	20070104	US 2006-559694	20060501

PRIORITY APPLN. INFO.: DE 2003-10325813 A 20030606
WO 2004-EP6014 W 20040603

AB The invention discloses a medicament for the prophylaxis and/or treatment of diseases or complications associated with portal hypertension, especially hemorrhagic complications. The invention uses a phosphodiesterase V inhibitor, e.g. sildenafil.

L8 ANSWER 2 OF 10 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004526367 EMBASE
TITLE: Pulmonary arterial hypertension: Newer treatment are improving outcomes.
AUTHOR: Sirithanakul K.; Mubarak K.K.
CORPORATE SOURCE: Dr. K.K. Mubarak, Wayne State University, 3990 John R, 3937 Hudson, Detroit, MI 48201, United States. mubarak@wayne.edu
SOURCE: Journal of Family Practice, (Dec 2004) Vol. 53, No. 12, pp. 959-969.
Refs: 59
ISSN: 0094-3509 CODEN: JFAPDE
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Clinical and Experimental Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

ENTRY DATE: Entered STN: 30 Dec 2004
Last Updated on STN: 30 Dec 2004

L8 ANSWER 3 OF 10 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005064723 EMBASE
TITLE: Gateways to clinical trials: December 2004.
AUTHOR: Bayes M.; Rabasseda X.; Prous J.R.
CORPORATE SOURCE: M. Bayes, Prous Science, P.O. Box 540, 08080 Barcelona, Spain. mbayes@prous.com
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (Dec 2004) Vol. 26, No. 10, pp. 801-827.
Refs: 163
ISSN: 0379-0355 CODEN: MFEPDX
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Feb 2005
Last Updated on STN: 24 Feb 2005
AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies Knowledge Area of Prous Science Integrity®, the drug discovery and development portal , http://integrity. prous.com. This issue focuses on the following selection of drugs: Abetimus sodium, ademetionine, agalsidase alfa, agalsidase beta, alemtuzumab, alfimeprase, AMG-162, androgel, anidulafungin, antigastrin therapeutic vaccine, aripiprazole, atomoxetine hydrochloride; Bazedoxifene acetate, bevacizumab, bosentan; Caldaret hydrate, canfosfamide hydrochloride, choriogonadotropin alfa, ciclesonide, combretastatin A-4 phosphate, CY-2301; Darbepoetin alfa, darifenacin hydrobromide, decitabine, degarelix acetate, duloxetine hydrochloride; ED-71, enclomiphene citrate, eplerenone, epratuzumab, escitalopram oxalate, eszopiclone, ezetimibe; Fingolimod hydrochloride, FP-1096; HMR-3339A, HSV-TK/GCV gene therapy, human insulin, HuOKT3gamma1(Ala234-Ala235); Idursulfase, imatinib mesylate, indiplon, InnoVax C insulin glargine, insulin glulisine, irofulven; Labetuzumab, lacosamide, lanthanum carbonate, LyphoDerm, Lyprinol; Magnesium sulfate, metelimumab, methylphenidate hydrochloride; Natalizumab, NO-aspirin; OROS(R); PC-515, pegaptanib sodium, peginterferon alfa-2a, peginterferon alfa-2b, peginterferon alfa-2b/ribavirin, pemetrexed disodium, peptide YY3-36, posaconazole, pregabalin, PT-141, pyridoxamine; R-744, ramelteon, ranelic acid distrontium salt, rebimastat, repinotan hydrochloride, rhC1, rhGAD65, rosiglitazone maleate/metformin hydrochloride; Sardomozide, solifenacin succinate; Tadalafil, taxus, telavancin, telithromycin, tenofovir disoproxilfumarate, teriparatide, testosterone transdermal patch, tetomilast, tirapazamine, torcetrapib; Valspodar, vardenafil hydrochloride hydrate, vildagliptin; Yttrium Y90 epratuzumab; Ziprasidone hydrochloride. .COPYRGT. 2004 Prous Science. All rights reserved.

L8 ANSWER 4 OF 10 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005024582 EMBASE
TITLE: Gateways to Clinical Trials.
AUTHOR: Bayes M.; Rabasseda X.; Prous J.R.
CORPORATE SOURCE: M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain. mbayes@prous.com

SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (Nov 2004) Vol. 26, No. 9, pp. 723-753.
Refs: 195
ISSN: 0379-0355 CODEN: MFEPDX
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
006 Internal Medicine
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jan 2005
Last Updated on STN: 6 Sep 2007

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Trials Knowledge Area of Prous Science Integrity(R), the drug discovery and development portal, http://integrity.prous.com. This issue focuses on the following selection of drugs: (PE)HRG214, 1E10, 21-Aminoepothilone B; Ad.Egr.TNF.11D, Ad110-B7.1/HLA, adalimumab, adefovir dipivoxil, alefacept, alemtuzumab, AMD-070, anhydrovinblastine, aripiprazole, asimadoline, atrasentan, AVE-5883; Bimatoprost, BNP-7787, bosentan, botulinum toxin type B, BR-1; Canfosfamide hydrochloride, ciclesonide, curcumin, cypher; D0401, darbepoetin alfa, darifenacin hydrobromide, D-D4FC, dendritic cell-based vaccine, desloratadine, dextrin sulfate, dolastatin 10, drospirenone drospirenone/estradiol, DS-992, duloxetine hydrochloride, dutasteride; E-7010, efalizumab, eletriptan, EM-1421, enfuvirtide, entecavir, etoricoxib, everolimus, exenatide, ezetimibe; Favid, fidarestat, fingolimod hydrochloride, FK-352; Gefitinib, gemifloxacin mesilate, gepirone hydrochloride, gimatecan; HE-2000; Imatinib mesylate, indisulam, insulin detemir, irofulven, ISIS-5132; Lapatinib, levocetirizine, liraglutide, lumiracoxib; Metformin/Glyburide, methionine enkephalin, MK-0431, morphine hydrochloride, motexafin gadolinium, mycobacterium cell wall complex; Naturasone, neridronic acid, nesiritide; Oblimersen sodium, olanzapine/fluoxetine hydrochloride, omalizumab, oral insulin; Paclitaxel poliglumex, PC-515, PEG-filgrastim, peginterferon alfa-2a, peginterferon alfa-2b, peginterferon alfa-2b/ribavirin, pegvisomant, pexelizumab, picoplatin, pramlintide acetate, prasterone, pregabalin; Quercetin; Ramelteon, ranirestat, RG228, rhGAD65, roflumilast, rubitecan; Sitaxsentan sodium, solifenacin succinate; Tadalafil, taxus, tipifarnib, tolevamer sodium, topixantrone hydrochloride; Valganciclovir hydrochloride, vardenafil hydrochloride hydrate, vildagliptin, voriconazole; XTL-001; Zoledronic acid monohydrate.

L8 ANSWER 5 OF 10 EMBASE
ACCESSION NUMBER: 2004349672 EMBASE
TITLE: Gateways to Clinical Trials: July/August 2004.
AUTHOR: Bayes M.; Rabasseda X.; Prous J.R.
CORPORATE SOURCE: M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain. mbayes@prous.com
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (Jul 2004) Vol. 26, No. 6, pp. 473-503.
Refs: 194
ISSN: 0379-0355 CODEN: MFEPDX
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology

037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Sep 2004
Last Updated on STN: 16 Sep 2004
AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Trials Knowledge Area of Prous Science Integrity®, the drug discovery and development portal , http://integrity. prous.com. This issue focuses on the following selection of drugs: ABI-007, Ad.Egr.TNF.11D, adefovir dipivoxil, AdPEDF.11, AES-14, albumex, alefacept, alemtuzumab, aliskiren fumarate, alvimopan hydrate, aAminolevulinic acid hydrochloride, aminolevulinic acid methyl ester, anakinra, anti-IL-12 MAb, aprepitant, atazanavir sulfate, atrasentan, avanafil; Banoxantrone, BG-12, bimatoprost, bortezomib, bosentan; Calcipotriol/betamethasone dipropionate, caspofungin acetate, CBT-1, ciclesonide, clofarabine, conivaptan hydrochloride, CpG-7909, C-Vax, Cypher; DA-8159, DAC:GLP-1, darbepoetin alfa, darifenacin, duloxetine hydrochloride; Eculizumab, efalizumab, efaproxiral sodium, EGF vaccine, eletriptan, epratuzumab, erlotinib hydrochloride, escitalopram oxalate, ETC-642, etoricoxib, everolimus, exenatide; Gefitinib, IV gamma-globulin; Human insulin, gamma-hydroxybutyrate sodium; IDN-6556, iguratimod, imatinib mesylate, indiplon, ixabepilone; Laquinimod, LB-80380, lidocaine/prilocaineliraglutide, lopinavir, lopinavir/ritonavir, lucinactant; MAb-14.18, melatonin, MLN-591-DM1; NC-531, neridronic acid, nesiritide, neutrophil-inhibitory factor, niacin/lovastatin niacinllovastatin; Oblimersen sodium, olcegepant, oral Insulin, ORV-105; Palonosetron hydrochloride, PAmAb, pegaptanib sodium, peginterferon alfa-2a, pegvisomant, perifosine, pexelizumab, phenoxodiol, phenserine tartrate, pimecrolimus, pramlintide acetate, pregabalin, PRO-542, prostate cancer vaccine, PT-141; Ramelteon, rasagiline mesilate, rDNA insulin, reslizumab, rh-Lactoferrin, ribamidine hydrochloride, rosuvastatin calcium; S-8184l, SC-1, sorafenib, St. John's Wort extract, SU-11248; Taxus, telbivudine, tenofovir disoproxil fumarate, teriparatide, testosterone gel, tezosentan disodium, tipifarnib, tolvaptan, trabectedin, travoprost, travoprost/timolol, treprostinil sodium; Vardenafil hydrochloride hydrate; Xcellerated T cells, XR-5944; Yttrium 90 (90Y) ibritumomab tiuxetan; Ziconotide.

L8 ANSWER 6 OF 10 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:356876 BIOSIS
DOCUMENT NUMBER: PREV200510148043
TITLE: Phosphodiesterase-5 (PDE-5) is up-regulated in cirrhotic rat livers; Potential role for PDE-5 inhibitors in reducing the increased intrahepatic vascular tone in cirrhosis.
AUTHOR(S): Loureiro-Silva, Mauricio [Reprint Author]; Iwakiri, Yasuko; Abraldes, Juan G.; Haq, Omar; Groszmann, Roberto J.
CORPORATE SOURCE: Yale Univ, Sch Med, VAMC, New Haven, CT USA
SOURCE: Hepatology, (OCT 2004) Vol. 40, No. 4, Suppl. 1, pp. 271A.
Meeting Info.: 55th Annual Meeting of the American-Association-for-the-Study-of-Liver-Diseases (AASLD). Boston, MA, USA. October 29 -November 02, 2004. Amer Assoc Study Liver Dis.
CODEN: HPTLD9. ISSN: 0270-9139.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Sep 2005

Last Updated on STN: 14 Sep 2005

L8 ANSWER 7 OF 10 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004159928 EMBASE
TITLE: Gateways to Clinical Trials.
AUTHOR: Bayes M.; Rabasseda X.; Prous J.R.
CORPORATE SOURCE: M. Bayes, Prous Science, P.O. Box 540, 08080 Barcelona, Spain. mbayes@prous.com
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (Mar 2004) Vol. 26, No. 2, pp. 129-161.
Refs: 229
ISSN: 0379-0355 CODEN: MFEPDX
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 May 2004
Last Updated on STN: 13 May 2004

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies Knowledge Area of Prous Science Integrity(R), the drug discovery and development portal, http://integrity.prous.com. This issue focuses on the following selection of drugs: Activated protein C concentrate, Ad-CD154, Adeno-Interferon gamma, alemtuzumab, APC-8024, 9-aminocamptothecin, aprepitant, L-arginine hydrochloride, aripiprazole, arsenic trioxide, asimadoline; O6-Benzylguanine, bevacizumab, Bi-20, binodenoson, biphasic insulin aspart, bivatuzumab, 186Re-bivatuzumab, BMS-181176, bosentan, botulinum toxin type B, BQ-123, bryostatin 1; Carboxyamidotriazole, caspofungin acetate, CB-1954, CC-4047, CDP-860, cerivastatin sodium, clevidipine, CTL-102; 3,4-DAP, darbepoetin alfa, decitabine, desloratadine, DHA-paclitaxel, duloxetine hydrochloride; Efalizumab, EGF vaccine, eletriptan, eniluracil, ENMD-0997, eplerenone, eplivanserin, erlosamide, ertapenem sodium, escitalopram oxalate, esomeprazole magnesium, eszopiclone, everolimus, exatecan mesilate, exenatide, ezetimibe; Fondaparinux sodium, FR-901228, FTY-720; Gefitinib, gemtuzumab ozogamicin, gepirone hydrochloride; Hexyl insulin M2, human insulin; Imatinib mesylate, insulin detemir, insulin glargine, iodine (I131) tositumomab, ISV-205, ivabradine hydrochloride, ixabepilone; Levetiracetam, levocetirizine, linezolid, liposomal NDDP, lonafarnib, lopinavir, LY-156735; Mafosfamide cyclohexylamine salt, magnesium sulfate, maxacalcitol, meclinertant, melagatran, melatonin, MENT, mepolizumab, micafungin sodium, midostaurin, motexafin gadolinium; Nesiritide, NS-1209, NSC-601316, NSC-683864; Osanetant; Palonosetron hydrochloride, parecoxib sodium, pegaptanib sodium, peginterferon alfa-2a, peginterferon alfa-2b, pegylated OB protein, pemetrexed disodium, perillyl alcohol, picoplatin, pimecrolimus, pixantrone maleate, plevitrexed, polyglutamate paclitaxel, posurdex, pramlintide acetate, prasterone, pregabalin; Rasburicase, rimonabant hydrochloride, rostaporfin, rosuvastatin calcium; SDZ-SID-791, sibrotuzumab, sorafenib, SU-11248; Tadalafil, targinine, tegaserod maleate, telithromycin, TheraCIM, tigecycline, tiotropium bromide, tipifarnib, tirapazamine, treprostinil sodium; Valdecoxib, Valganciclovir hydrochloride, Vardenafil hydrochloride hydrate; Ximelagatran; Zofenopril calcium, Zoledronic acid monohydrate. .COPYRGT. 2004 Prous Science. All rights reserved.

L8 ANSWER 8 OF 10 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:286345 BIOSIS
DOCUMENT NUMBER: PREV200400285102

TITLE: Role of phosphodiesterase-5 (PDE5) in altered vascular reactivity in cirrhotic rats.
AUTHOR(S): Sabra, Ramzi [Reprint Author]; Tahseldar-Roumieh, Rima; Ghali, Rana; Tumeh, Yara; El-Hajj, Ihab; Lugnier, Claire
CORPORATE SOURCE: Pharmacology, American University of Beirut, Bliss Strees, Beirut, -, -, Lebanon
rsabra@aub.edu.lb
SOURCE: FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 643.9. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jun 2004
Last Updated on STN: 16 Jun 2004

AB Previous studies showed increased PDE5 activity in kidneys of cirrhotic rats, which might explain the reduced response to natriuretic peptides and the Na retention observed in cirrhosis.We examined if changes in PDE5 can cause altered vascular reactivity in cirrhotic rats. Methods: Cirrhosis was induced by bile duct ligation and excision (BDL). Four weeks after BDL or sham operation (Sham), a concentration response curve fro nitroglycerine (NG) was obtained in endothelium denuded vascular rings from thoracic aortae precontracted with phenylephrine (PE). In some experiments, the rings were pre-incubated with 0.1muM DMPPO, a selective inhibitor of PDE5. In similar experiments, a concentration response curve was ontained for DMPPO. Expression of PDE5 was studied in aortas, kidneys and mesenteric vessels of BDL and Sham rats. Results: The NG curve was right-shifted in BDL rats; pre-incubation with DMPPO enhanced the vasodilator responses in all groups and eliminated the differences in sensitivity between Sham and BDL (see figure). Similarly, the DMPPO concnetration—response curve was right shifted in BDL rats. Expression of PDE5 protein was increased in the aorta and decreased in the mesenteric vasculature in BDL vs. Sham. Conclusions: In cirrhotic animals, the reduced sensitivity of the aortic rings to an NO donor may be explained by higher PDE5 activity in the aorta, leading to a less cGMP levels in response NO (NG). The attenuation of the vasodilator responses to DMPPO and the increased PDE5 expresion in the aorta of BDL rats supports this conclusion. These results may indicate an important role for changes in PDE5 activity in the hemodynamic changes that occur in cirrhosis and portal hypertension; the relation between PDE5 and vasodilation in the splanchnic bed is being explored.Supported by a grant from the Lebanese National Council for Scientific Research.. .

L8 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:590998 CAPLUS
DOCUMENT NUMBER: 139:128037
TITLE: Use of acetylcholine esterase antagonists to treat insulin resistance
INVENTOR(S): Lautt, Wayne W.
PATENT ASSIGNEE(S): Diamedica Inc., Can.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003061648	A1	20030731	WO 2003-CA78	20030127 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003235609	A1	20031225	US 2003-350478	20030124 <--
CA 2514088	A1	20030731	CA 2003-2514088	20030127 <--
EP 1471905	A1	20041103	EP 2003-700275	20030127 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005519906	T	20050707	JP 2003-561592	20030127
US 2005049293	A1	20050303	US 2004-502066	20041027
PRIORITY APPLN. INFO.:			US 2002-350958P	P 20020125
			WO 2003-CA78	W 20030127

AB A method is provided for reducing insulin resistance in a mammalian subject, comprising administering a suitable acetylcholine esterase antagonist.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 10 EMBASE

ACCESSION NUMBER: 2003256920 EMBASE
TITLE: Gateways to clinical trials: May 2003.
AUTHOR: Bayes M.; Rabasseda X.; Prous J.R.
CORPORATE SOURCE: M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona, Spain. mbayes@prous.com
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology, (May 2003) Vol. 25, No. 4, pp. 317-340.
Refs: 143
ISSN: 0379-0355 CODEN: MFEPDX
COUNTRY: Spain
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jul 2003
Last Updated on STN: 17 Jul 2003

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies knowledge area of Prous Science Integrity®, the drug discovery and development portal , http://integrity.prous.com. This issue focuses on the following selection of drugs: 2F5, 2G12, Abetimus sodium, ABI-007, adalimumab, adefovir dipivoxil, AE-941, alefacept, altropane, aminolevulinic acid hydrochloride, aminolevulinic acid methyl ester, aminopterin, anakinra, aprinocarsen sodium, atazanavir, atlizumab, atomoxetine hydrochloride; B7-1 vaccine, bevacizumab, biricodar dicitrate, BMS-188667, brasofensine sulfate, bryostatin 1; Cantuzumab mertansine, CHS-828, cinacalcet hydrochloride, cipamfylline, creatine, CVT-3146; Darbepoetin alfa, DITPA, drotrecogin alfa (activated), duloxetine hydrochloride; Edatrexate, efalizumab, ENMD-0997, epoetin, erlosamide, esomeprazole magnesium, etiprednol dicloacetate, etoricoxib, everolimus, ezetimibe; Fampridine, fenretinide, FTY-720; IGF-I/IGFBP-3 IL-1 cytokine trap, ilodecakin,

interferon beta, ISIS-104838, ISIS-2503, ISIS-5132, ivabradine hydrochloride; Lafutidine, lanthanum carbonate, L-Arginine hydrochloride, LEA29Y, lerdelimumab, levetiracetam, levobupivacaine hydrochloride, levosimendan, lopinavir; Melagatran, mibefradil hydrochloride, miglustat, morphine-6-glucuronide; Nesiritide; Omalizumab, omapatrilat; p24-VLP, parecoxib sodium, peginterferon alfa-2a, peginterferon alfa-2b, pegsunercept, pitavastatin calcium, plevitrexed, prasterone, pregabalin, PRO-2000, prucalopride; Rapacuronium bromide, rebimastat, RGA-0853, rubitecan, ruboxistaurin mesilate hydrate, RWJ-67657; S-16020-2, sarizotan, SLV-306, stiripentol; TA-CIN, tenecteplase, teriparatide, tezacitabine, tipifarnib, trabectedin, troglitazone; Valdecoxib, vardenafil; Z-338, ziconotide.

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NEWS 3	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS 4	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS 5	JUL 28	STN Viewer performance improved
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NEWS 7	AUG 13	CA/CAplus enhanced with printed Chemical Abstracts page images from 1967-1998
NEWS 8	AUG 15	CAOLD to be discontinued on December 31, 2008
NEWS 9	AUG 15	CAplus currency for Korean patents enhanced
NEWS 10	AUG 27	CAS definition of basic patents expanded to ensure comprehensive access to substance and sequence information
NEWS 11	SEP 18	Support for STN Express, Versions 6.01 and earlier, to be discontinued
NEWS 12	SEP 25	CA/CAplus current-awareness alert options enhanced to accommodate supplemental CAS indexing of exemplified prophetic substances
NEWS 13	SEP 26	WPIDS, WPINDEX, and WPIX coverage of Chinese and and Korean patents enhanced
NEWS 14	SEP 29	IFICLS enhanced with new super search field
NEWS 15	SEP 29	EMBASE and EMBAL enhanced with new search and display fields
NEWS 16	SEP 30	CAS patent coverage enhanced to include exemplified prophetic substances identified in new Japanese-language patents
NEWS 17	OCT 07	EPFULL enhanced with full implementation of EPC2000
NEWS 18	OCT 07	Multiple databases enhanced for more flexible patent number searching
NEWS 19	OCT 22	Current-awareness alert (SDI) setup and editing

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                  enhanced
 NEWS 20  OCT 22  WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT
                  Applications
 NEWS 21  OCT 24  CHEMLIST enhanced with intermediate list of
                  pre-registered REACH substances

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

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=> s portal (s) (hypertens? or pressure)
L1       20994 PORTAL (S) (HYPERTENS? OR PRESSURE)

=> s (phosphodiesterase or pde) (s) (5 or five)
L2       17871 (PHOSPHODIESTERASE OR PDE) (S) (5 OR FIVE)

=> s l1 and l2
L3          20 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           19 DUP REM L3 (1 DUPLICATE REMOVED)

=> s l4 and py<=2003
L5           1 L4 AND PY<=2003

=> d l5 ibib abs

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        1995:396408  CAPLUS
DOCUMENT NUMBER:         122:157633
ORIGINAL REFERENCE NO.:  122:29029a,29032a
TITLE:                   Change in vascular cAMP and cGMP contents in
                         portal hypertensive rats
```

AUTHOR(S): Huang, Yi-Tsau; Lo, Jeng-Wu; Lin, Han-Chieh; Tsai, Yang-Te; Hong, Chaung-Ye; Yang, May C. M.
CORPORATE SOURCE: Institute Traditional Medicine, National Yang Ming Medical College, Taipei, Taiwan
SOURCE: Pharmacology (1995), 50(2), 86-91
CODEN: PHMGBN; ISSN: 0031-7012
PUBLISHER: Karger
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to investigate the possible changes of cyclic nucleotide contents in portal hypertensive rats. Portal hypertension was induced by partial portal vein ligation (PVL) in Sprague-Dawley rats. Sham-operated rats served as controls. Hemodynamic and cyclic nucleotide measurements were performed at 14 days after surgery. The portal venous pressure was significantly higher, while systemic arterial pressure and heart rate were lower in PVL rats than those in controls. Basal cAMP (PVL, 10.91 ± 0.98, vs. sham, 8.08 ± 0.81 pmol/mg protein) and cGMP (PVL, 0.91 ± 0.12, vs. sham, 0.59 ± 0.05 pmol/mg protein) contents in the tail artery were significantly higher in PVL rats. Isobutyryl methylxanthine (10-5 M), a nonspecific phosphodiesterase inhibitor, exerted similarly stimulating effects on the tissue cAMP (PVL, 158 ± 10, vs. sham, 178 ± 20%) and cGMP (295 ± 28 vs. 316 ± 71%) levels in both PVL and control rats; so did forskolin (10-6 M) on the cAMP (184 ± 20 vs. 197 ± 66%) content in both groups. Our results showed that the arterial cAMP and cGMP contents were higher in PVL rats, which may contribute to the reduction of peripheral resistance in portal hypertension.

=> s portal and hypertension and phosphodiesterase
L6 38 PORTAL AND HYPERTENSION AND PHOSPHODIESTERASE

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 36 DUP REM L6 (2 DUPLICATES REMOVED)

=> s l7 and py<=2003
L8 5 L7 AND PY<=2003

=> d l8 ibib abs 1-5

L8 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:590998 CAPLUS
DOCUMENT NUMBER: 139:128037
TITLE: Use of acetylcholine esterase antagonists to treat insulin resistance
INVENTOR(S): Lautt, Wayne W.
PATENT ASSIGNEE(S): Diamedica Inc., Can.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061648	A1	20030731	WO 2003-CA78	20030127 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 20030235609	A1	20031225	US 2003-350478		20030124 <--
CA 2514088	A1	20030731	CA 2003-2514088		20030127 <--
EP 1471905	A1	20041103	EP 2003-700275		20030127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005519906	T	20050707	JP 2003-561592		20030127
AU 2003201578	B2	20080306	AU 2003-201578		20030127
US 20050049293	A1	20050303	US 2004-502066		20041027
PRIORITY APPLN. INFO.:			US 2002-350958P	P	20020125
			WO 2003-CA78	W	20030127

AB A method is provided for reducing insulin resistance in a mammalian subject, comprising administering a suitable acetylcholine esterase antagonist.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:396408 CAPLUS
DOCUMENT NUMBER: 122:157633
ORIGINAL REFERENCE NO.: 122:29029a,29032a
TITLE: Change in vascular cAMP and cGMP contents in portal hypertensive rats
AUTHOR(S): Huang, Yi-Tsau; Lo, Jeng-Wu; Lin, Han-Chieh; Tsai, Yang-Te; Hong, Chaung-Ye; Yang, May C. M.
CORPORATE SOURCE: Institute Traditional Medicine, National Yang Ming Medical College, Taipei, Taiwan
SOURCE: Pharmacology (1995), 50(2), 86-91
CODEN: PHMGBN; ISSN: 0031-7012
PUBLISHER: Karger
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to investigate the possible changes of cyclic nucleotide contents in portal hypertensive rats. Portal hypertension was induced by partial portal vein ligation (PVL) in Sprague-Dawley rats. Sham-operated rats served as controls. Hemodynamic and cyclic nucleotide measurements were performed at 14 days after surgery. The portal venous pressure was significantly higher, while systemic arterial pressure and heart rate were lower in PVL rats than those in controls. Basal cAMP (PVL, 10.91 ± 0.98, vs. sham, 8.08 ± 0.81 pmol/mg protein) and cGMP (PVL, 0.91 ± 0.12, vs. sham, 0.59 ± 0.05 pmol/mg protein) contents in the tail artery were significantly higher in PVL rats. Isobutyryl methylxanthine (10-5 M), a nonspecific phosphodiesterase inhibitor, exerted similarly stimulating effects on the tissue cAMP (PVL, 158 ± 10, vs. sham, 178 ± 20%) and cGMP (295 ± 28 vs. 316 ± 71%) levels in both PVL and control rats; so did forskolin (10-6 M) on the cAMP (184 ± 20 vs. 197 ± 66%) content in both groups. Our results showed that the arterial cAMP and cGMP contents were higher in PVL rats, which may contribute to the reduction of peripheral resistance in portal hypertension.

L8 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1984:32896 CAPLUS
DOCUMENT NUMBER: 100:32896
ORIGINAL REFERENCE NO.: 100:5091a,5094a

TITLE: Effects of sodium-decreased media on tonus and of spasmolytics on the responses to contractile agents in portal veins from SHRSP and WKY [rats]
AUTHOR(S): Murakami, Noriko; Niwa, Atsuko; Higashino, Hideaki; Suzuki, Aritomo
CORPORATE SOURCE: Sch. Med., Kinki Univ., Osaka, 659, Japan
SOURCE: Vasc. Neuroeff. Mech., Int. Symp., 4th (1983), Meeting Date 1981, 413-16. Editor(s): Bevan, John A. Raven: New York, N. Y.
CODEN: 50PUAW
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Isometric contractions of portal vein sections from stroke-prone spontaneously hypertensive rats (SHRSP) (induced by acetylcholine, norepinephrine, KCl, or BaCl2) were inhibited by dibutyryl cAMP, aminophylline (a phosphodiesterase inhibitor), or fenoterol (a β-stimulant) less than the vein sections from normal control Wistar Kyoto rats (WKY). Diltiazem (a Ca antagonist) inhibited the contractions in SHRSP more than in control WKY rats. The replacement of normal incubation medium (Locke's solution) by medium with low Na and(or) Ca concns. caused stronger contractions in SHRSP than in WKY controls. Thus, in SHRSP portal veins, the reactivity to cAMP is decreased; the reactivity of β-receptors is impaired; and Ca transport into cells and/or Ca release from cell stores are accelerated as compared with those of WKY rats.

L8 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1975:84098 CAPLUS
DOCUMENT NUMBER: 82:84098
ORIGINAL REFERENCE NO.: 82:13468h,13469a
TITLE: Cyclic AMP [of] blood vessels of spontaneously hypertensive rat
AUTHOR(S): Ramanathan, S.; Shibata, Shoji
CORPORATE SOURCE: Sch. Med., Univ. Hawaii, Honolulu, HI, USA
SOURCE: Blood Vessels (1974), 11(5), 312-18
CODEN: BLVSAB; ISSN: 0303-6847
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The vascular smooth muscle (aorta, portal vein, and renal arteries) from spontaneously hypertensive rats (SHR) contained a lower level of cyclic AMP. Similar differences were observed in young SHR that had not yet developed hypertension, as compared to their normotensive controls. However, no such difference was observed in the vascular smooth muscle from the cross-bred normotensive animals. The adenyl cyclase and phosphodiesterase activities of the vascular smooth muscles from SHR was lower than the normotensive controls. Changes in cyclic AMP metabolism may occur during the process of hypertension.

L8 ANSWER 5 OF 5 MEDLINE on STN
ACCESSION NUMBER: 2003179790 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12644956
TITLE: Pulmonary hypertension.
AUTHOR: Nicod Laurent P
CORPORATE SOURCE: Pulmonary division, University Hospital, Geneva, Switzerland.. laurent.nicod@hcuge.ch
SOURCE: Swiss medical weekly : official journal of the Swiss Society of Infectious Diseases, the Swiss Society of Internal Medicine, the Swiss Society of Pneumology, (2003 Feb 22) Vol. 133, No. 7-8, pp. 103-10. Ref: 52
Journal code: 100970884. ISSN: 1424-7860.

PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 18 Apr 2003
Last Updated on STN: 28 Jun 2003
Entered Medline: 27 Jun 2003

AB Pulmonary arterial hypertension (PAH) must be classified into primary pulmonary hypertension and PAH related to other diseases such as collagen vascular diseases, HIV infection or portal hypertension. PAH must also be differentiated from other entities, in particular pulmonary hypertension secondary to thromboembolic diseases, requiring specific approaches. All PAH results in similar histological remodelling of pulmonary arteries, with thickening of the intima, proliferation of the media and plexogenic lesions. Today the physiopathology of these lesions is much better understood and has resulted in new therapies involving substances such as prostacyclins, endothelin receptor antagonists or phosphodiesterase inhibitors, aimed not only at dilating arteries but also at preventing their remodelling. Thromboendarterectomy, septostomy and transplantation remain the only option where medical treatment has failed.

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	47.68	47.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.00	-4.00

FILE 'REGISTRY' ENTERED AT 14:32:11 ON 29 OCT 2008

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 OCT 2008 HIGHEST RN 1067631-14-4
DICTIONARY FILE UPDATES: 28 OCT 2008 HIGHEST RN 1067631-14-4

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http://www.cas.org/support/stngen/stndoc/properties.html

=> e vardenafil

E1	10	VARDEL/BI
E2	26	VARDEN/BI

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E3           5 --> VARDENAFIL/BI
E4           1     VARDHAK/BI
E5           1     VARDHMAN/BI
E6          10     VARDONI/BI
E7           8     VARE/BI
E8           1     VARE1944/BI
E9           1     VARE1970/BI
E10          1     VARE1976/BI
E11          1     VARE1978/BI
E12          1     VARE1988/BI

=> s e3
L9           5 VARDENAFIL/BI

=> e sildenafil
E1           1     SILDATE/BI
E2           1     SILDEGRA/BI
E3          18 --> SILDENAFIL/BI
E4           1     SILDEW/BI
E5           6     SILDEX/BI
E6           1     SILDI/BI
E7           1     SILDITHAIZANE/BI
E8           1     SILDITHI/BI
E9           1     SILDITHIAZA/BI
E10          1     SILDITHIAZANE/BI
E11         47     SILE/BI
E12          1     SILECE/BI

=> s e3
L10         18 SILDENAFIL/BI

=> file medline caplus
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  10.76      58.65

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                   0.00      -4.00

FILE 'MEDLINE' ENTERED AT 14:32:48 ON 29 OCT 2008

FILE 'CAPLUS' ENTERED AT 14:32:48 ON 29 OCT 2008
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=> s (l9 or vardenafil or l10 or sildenafil) and portal and (pressure or hypertens?)
L11         22 (L9 OR VARDENAFIL OR L10 OR SILDENAFIL) AND PORTAL AND (PRESSUR
               E OR HYPERTENS?)

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12          20 DUP REM L11 (2 DUPLICATES REMOVED)

=> d l12 ibib abs 1-20

L12  ANSWER 1 OF 20     MEDLINE on STN
ACCESSION NUMBER:   2008156741     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 18306330
TITLE:              Safety and efficacy of combined use of sildenafil
                    , bosentan, and iloprost before and after liver
```

transplantation in severe portopulmonary hypertension.
AUTHOR: Austin Mark J; McDougall Neil I; Wendon Julia A; Sizer Elizabeth; Knisely Alex S; Rela Mohammed; Wilson Carol; Callender Michael E; O'Grady John G; Heneghan Michael A
CORPORATE SOURCE: Institute of Liver Studies, King's College Hospital, London, England.
SOURCE: Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society, (2008 Mar) Vol. 14, No. 3, pp. 287-91.
Journal code: 100909185. E-ISSN: 1527-6473.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200806
ENTRY DATE: Entered STN: 5 Mar 2008
Last Updated on STN: 6 Jun 2008
Entered Medline: 5 Jun 2008
AB Portopulmonary hypertension (PPHTN) represents a constrictive pulmonary vasculopathy in patients with portal hypertension. Liver transplantation (LT) may be curative and is usually restricted to patients with mild-to-moderate disease severity characterized by a mean pulmonary artery pressure (mPAP < 35 mm Hg). Patients with severe disease (mPAP > 50 mm Hg) are usually excluded from transplantation. We describe a patient with severe PPHTN, initiated on sequential and ultimately combination therapy of prostacyclin, sildenafil, and bosentan (PSB) pretransplantation and continued for 2 years posttransplantation. Peak mPAP on PSB therapy was dramatically reduced from 70 mm Hg to 32 mm Hg pretransplantation, and continued therapy facilitated a further fall in mPAP to 28 mm Hg posttransplantation. The pulmonary vascular resistance index fell from 604 to 291 dyne second(-1) cm(-5). The perioperative mPAP rose to 100 mm Hg following an episode of sepsis and fell with optimization of PSB therapy. In conclusion, this is the first reported patient with severe PPHTN using this combination of vasodilator therapy as a bridge to LT and then as maintenance in the posttransplantation phase. This regimen may enable LT in similar patients in the future, without long-term consequences.

L12 ANSWER 2 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2007497047 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17715635
TITLE: Hepatopulmonary syndrome and portopulmonary hypertension: what's new?.
AUTHOR: Colle Isabelle; Van Steenkiste Christophe; Geerts Anja; Van Vlierberghe Hans
CORPORATE SOURCE: Department of Hepatology and Gastroenterology, Ghent University Hospital, Ghent, Belgium..
Isabelle.Colle@ugent.be
SOURCE: Acta gastro-enterologica Belgica, (2007 Apr-Jun) Vol. 70, No. 2, pp. 203-9. Ref: 67
Journal code: 0414075. ISSN: 0001-5644.
PUB. COUNTRY: Belgium
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200710
ENTRY DATE: Entered STN: 25 Aug 2007

Last Updated on STN: 12 Oct 2007
Entered Medline: 11 Oct 2007

AB Hepatopulmonary syndrome (HPS) is found in 4-47% of patients with cirrhosis and is characterized by intrapulmonary vascular dilatations especially in the basal parts of the lung. Liver injury and/or portal hypertension trigger the release of endothelin-1, TNF-alpha, cytokines and mediate vascular shear stress and release of nitric oxide and carbon monoxide, all contributing to intrapulmonary vasodilation. Severe HPS increases mortality (30%) after liver transplantation, especially if Pa O2 is below 50 mmHg. The diagnosis is made by calculating the alveolar-arterial oxygen gradient and by performing a contrast echocardiography. Medical therapy fails and the only long-term treatment available is liver transplantation. More than 85% experience significant improvement or complete resolution in hypoxaemia, but this may take more than 1 year. Portopulmonary hypertension (PPHT) occurs in 2-8% of the patients with cirrhosis. Imbalance between vasodilating (decreased pulmonary expression of eNOS and prostacyclin I2) and vasoconstrictive agents (increased expression of ET-1 and angiotensin 1) may be responsible for misguided angiogenesis and pulmonary hypertension. The diagnosis is made by performing an echocardiography and a right heart catheterisation when systolic pulmonary artery pressure is higher than 30 mmHg on echocardiography. Although prostacyclin analogues are efficacious, adverse effects in terms of safety, tolerability and drug delivery occur. Bosentan is probably the therapy of choice for patients with PPHT because it decreases pulmonary but can also diminish portal hypertension. Sildenafil, a phosphodiesterase-5 inhibitor is used for idiopathic pulmonary hypertension, however, it should be used cautiously in patients with portal hypertension as it may increase portal hypertension by splanchnic vasodilation.

L12 ANSWER 3 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2007523904 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 17623085
TITLE: Phosphodiesterase 5 inhibitors lower both portal and pulmonary pressure in portopulmonary hypertension: a case report.
AUTHOR: Bremer Hinrich C; Kreisel Wolfgang; Roecker Kai; Dreher Michael; Koenig Daniel; Kurz-Schmieg Anna Katharina; Blum Hubert E; Roessle Martin; Deibert Peter
CORPORATE SOURCE: Department of Gastroenterology, Hepatology, Endocrinology and Infectious Diseases, University Hospital, Freiburg, Germany.. wolfgang.kreisel@uniklinik-freiburg.de
SOURCE: Journal of medical case reports, (2007) Vol. 1, pp. 46. Electronic Publication: 2007-07-10. Journal code: 101293382. E-ISSN: 1752-1947.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED
ENTRY DATE: Entered STN: 8 Sep 2007
Last Updated on STN: 8 Dec 2007

AB ABSTRACT: BACKGROUND: Portopulmonary hypertension (PPHTN) is a severe complication in liver cirrhosis. PDE5 inhibitors lower pulmonary arterial pressure (PAP) in PPHTN. However, their effect on portal hypertension has not yet been investigated. CASE PRESENTATION: A 55 year old male patient presented with PPHTN and alcoholic liver cirrhosis. 10 mg of Tadalafil, a PDE5 inhibitor with a long half-life, was administered orally under continuous monitoring of pulmonary and portal hemodynamics. For maintenance therapy the patient received Sildenafil 20 mg bid.Tadalafil lowered mean PAP from 45 to 39 mmHg within 60 minutes. Cardiac output (CO) increased from

6.8 to 7.9 l/min. Central venous pressure (CVP) remained stable at 3 mmHg. Systolic and diastolic blood pressure was lowered from 167/89 to 159/86 mmHg. Pulse rate increased from 75 to 87 per min. Wedged hepatic vein pressure (WHVP) decreased from 21 to 18 mm Hg, hepatovenous pressure gradient (HVPG) decreased from 10 to 7 mmHg. Hemodynamic monitoring after 6 months of Sildenafil therapy revealed a sustained lowering of mean PAP. HVPG remained constant at 10 mmHg. Cardiac and pulmonary performance had further improved. CONCLUSION: This case report shows for the first time, that phosphodiesterase 5 inhibitors lower both portal and pulmonary pressure in portopulmonary hypertension.

L12 ANSWER 4 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2006176244 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16555327
TITLE: Successful treatment of severe portopulmonary hypertension in a patient with Child C cirrhosis by sildenafil.
AUTHOR: Callejas Rubio Jose Luis; Salmeron Escobar Javier; Gonzalez-Calvin Jorge; Ortego Centeno Norberto
SOURCE: Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society, (2006 Apr) Vol. 12, No. 4, pp. 690-1.
Journal code: 100909185. ISSN: 1527-6465.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200609
ENTRY DATE: Entered STN: 30 Mar 2006
Last Updated on STN: 13 Sep 2006
Entered Medline: 12 Sep 2006

L12 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1123280 CAPLUS
DOCUMENT NUMBER: 145:449221
TITLE: Roflumilast and roflumilast N-oxide for the treatment of pulmonary hypertension, and combinations with phosphodiesterase 5 inhibitors
INVENTOR(S): Beume, Rolf; Hatzelmann, Armin; Marx, Degenhard; Schudt, Christian; Tenor, Hermann; Eddahibi, Saadia; Adnot, Serge
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 40pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006111495	A1	20061026	WO 2006-EP61557	20060412
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,				

VN, YU, ZA, ZM, ZW
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AU 2006237300	A1	20061026	AU 2006-237300	20060412
CA 2604295	A1	20061026	CA 2006-2604295	20060412
EP 1874309	A1	20080109	EP 2006-725734	20060412
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008536888	T	20080911	JP 2008-507056	20060412
MX 200712711	A	20080111	MX 2007-12711	20071012
CN 101163476	A	20080416	CN 2006-80013022	20071018
NO 2007005662	A	20071107	NO 2007-5662	20071107
IN 2007MN01889	A	20071207	IN 2007-MN1889	20071112
KR 2008002950	A	20080104	KR 2007-726282	20071112
PRIORITY APPLN. INFO.:			EP 2005-103147 A	20050419
			WO 2006-EP61557 W	20060412

AB The invention discloses the use of roflumilast, roflumilast-N-Oxide, or a pharmaceutically acceptable salt of either for the treatment of pulmonary hypertension. The invention addnl. discloses the use of roflumilast, roflumilast-N-oxide or a pharmaceutically acceptable salt of either in combination with a phosphodiesterase 5 inhibitor, or a pharmaceutically acceptable salt thereof, for the treatment of pulmonary hypertension.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:149404 CAPLUS
DOCUMENT NUMBER: 144:205821
TITLE: 2-Phenyl-substituted imidazotriazinone derivative phosphodiesterase 5 inhibitors for the treatment of symptoms treatable by increasing cGMP levels
INVENTOR(S): Haning, Helmut
PATENT ASSIGNEE(S): Bayer Healthcare A.-G., Germany
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006015715	A1	20060216	WO 2005-EP8057	20050723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
DE 102004038328	A1	20060316	DE 2004-102004038328	20040806
AU 2005270446	A1	20060216	AU 2005-270446	20050723

CA 2575907	A1	20060216	CA 2005-2575907	20050723
EP 1776120	A1	20070425	EP 2005-764196	20050723
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				
CN 101035539	A	20070912	CN 2005-80034023	20050723
JP 2008509101	T	20080327	JP 2007-524224	20050723
BR 2005014123	A	20080527	BR 2005-14123	20050723
IN 2007DN01126	A	20070427	IN 2007-DN1126	20070212
KR 2007041613	A	20070418	KR 2007-705245	20070305
NO 2007001231	A	20070503	NO 2007-1231	20070306
US 20070299088	A1	20071227	US 2007-659624	20070905
PRIORITY APPLN. INFO.:			DE 2004-102004038328A	20040806
			WO 2005-EP8057 W	20050723

OTHER SOURCE(S): MARPAT 144:205821

AB The invention relates to the use of PDE 5 inhibitors, and especially of known 2-phenyl-substituted imidazotriazinone derivs., for producing medicaments for the treatment of symptoms that can be treated by increasing cGMP levels in certain tissues, e.g. acute myocardial infarction and damage caused by reperfusion, various symptoms in the female and male reproductive system and urogenital tract, gastrointestinal diseases, damage caused by diabetes, and liver failure.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 20 MEDLINE on STN

ACCESSION NUMBER: 2006429328 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16856046
TITLE: Endothelin receptor antagonists for pulmonary arterial hypertension.
AUTHOR: Liu C; Chen J
CORPORATE SOURCE: Monash University, Australasian Cochrane Centre, Locked Bag 29, Clayton, VIctoria, Australia 3168.. lcwv@sohu.com
SOURCE: Cochrane database of systematic reviews (Online), (2006) Vol. 3, pp. CD004434. Electronic Publication: 2006-07-19.
Ref: 42
Journal code: 100909747. E-ISSN: 1469-493X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(META-ANALYSIS)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 21 Jul 2006
Last Updated on STN: 17 Oct 2006
Entered Medline: 16 Oct 2006

AB BACKGROUND: Pulmonary arterial hypertension (PAH) is a devastating disease, which leads to right heart failure and premature death. Pulmonary arterial hypertension can be classified into five categories according to Venice classification: (1) Idiopathic PAH; (2) Familial PAH; (3) PAH associated with collagen vascular disease, congenital systemic-to-pulmonary shunts, portal hypertension, HIV infection, drugs and toxins or other (thyroid disorders, glycogen storage disease, Gaucher disease, hereditary hemorrhagic telangiectasia, hemoglobinopathies, myeloproliferative disorders, splenectomy); (4) PAH associated with significant venous or capillary involvement, which includes pulmonary veno-occlusive disease (PVOD) and pulmonary capillary hemangiomatosis (PCH); (5) Persistent pulmonary hypertension of the newborn. PAH can also be secondary to chronic hypoxic lung disease as part of the "cor-pulmonale" syndrome, and also secondary to left sided heart disease, but these conditions are usually distinguished from those listed here. OBJECTIVES:

To evaluate the efficacy of endothelin receptor antagonists in pulmonary arterial hypertension. SEARCH STRATEGY: A search was carried out using the CENTRAL (Cochrane Central Register of Controlled Trials), MEDLINE, EMBASE, and the reference section of retrieved articles. Searches are current as of August 2005. SELECTION CRITERIA: Randomised controlled trials (RCTs) or quasi-randomised controlled trials involving patients with pulmonary arterial hypertension (PAH) were selected by two reviewers. DATA COLLECTION AND ANALYSIS: Two reviewers independently selected studies; assessed study quality; and extracted data. We analysed outcomes as continuous and dichotomous data. MAIN RESULTS: In this updated version of the review, we added two RCTs. Altogether, five RCTs met the entry criteria of the review (reporting eight group comparisons). The studies were of short duration (12-16 weeks), recruiting a total of 482 participants. Three studies compared a non-selective ERA (bosentan) with placebo, one compared bosentan with sildenafil (a phosphodiesterase inhibitor) , and one compared a selective ERA (sitaxsentan) with placebo. Over a 12-16 week period ERAs improved exercise capacity, improve Borg dyspnoea score, some measures of cardiopulmonary haemodynamics (pulmonary artery pressure, pulmonary vascular resistance, and cardiac index) in symptomatic patients with mainly idiopathic PAH. The effect of ERAs on mortality was not significant. The most severe side effect, hepatic toxicity, was not common. AUTHORS' CONCLUSIONS: ERAs in conjunction with conventional therapy over 12 to 16 weeks can improve exercise capacity, Borg dyspnoea scores and several cardiopulmonary haemodynamics variables in patients mainly with idiopathic PAH. The data on mortality do not currently show a benefit of this class of drugs on this endpoint. Additional assessment of this outcome is important in order to establish whether there is evidence that ERAs have an impact on the risk of death. Longer studies are required.

L12 ANSWER 8 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2006614048 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17048047
TITLE: Portopulmonary hypertension.
AUTHOR: Halank Michael; Ewert Ralf; Seyfarth Hans-Juergen; Hoeffken Gert
CORPORATE SOURCE: Carl Gustav Carus University Dresden, Internal Medicine I, Fetscherstr. 74, 01307 Dresden, Germany.
SOURCE: Journal of gastroenterology, (2006 Sep) Vol. 41, No. 9, pp. 837-47. Ref: 86
Journal code: 9430794. ISSN: 0944-1174.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200701
ENTRY DATE: Entered STN: 19 Oct 2006
Last Updated on STN: 10 Jan 2007
Entered Medline: 9 Jan 2007

AB Portopulmonary hypertension (PPHT) is defined as precapillary pulmonary hypertension accompanied by hepatic disease or portal hypertension. Pulmonary hypertension results from excessive pulmonary vascular remodeling and vasoconstriction. These histological alterations have been indistinguishable from those of other forms of pulmonary arterial hypertension. Factors involved in the pathogenesis of PPHT include volume overload, hyperdynamic circulation, and circulating vasoactive mediators. The disorder has a substantial impact on survival and requires focused treatment. Liver transplantation in patients with moderate to severe PPHT is associated with a significantly reduced survival rate. The best medical treatment

for patients with PPHT is controversial; most authors currently regard continuous intravenous application of prostacyclin as the treatment of choice for patients with severe PPHT. There is only very limited reported experience with inhaled prostacyclin or its analog, iloprost. Increasing evidence of the efficacy of the endothelin-receptor antagonist bosentan and of the phosphodiesterase-5 inhibitor sildenafil is emerging in highly selected patients with PPHT. In the future, a combination therapy of the above-mentioned agents might become a therapeutic option. Other agents such as beta-blockers seem to be harmful to patients with moderate to severe portopulmonary hypertension. Up-to-date, randomized, double-blind, controlled clinical trials are lacking and are needed urgently.

L12 ANSWER 9 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2007007757 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17202968
TITLE: [Porto-pulmonary hypertension]. Hypertension portopulmonaire.
AUTHOR: Chabot F; Gomez E; Boyer L; Kheir A; Le Pavec J; Sitbon O; Herve P
CORPORATE SOURCE: Service des Maladies Respiratoires et Reanimation Respiratoire, CHU Nancy, Universite Henri Poincare, Nancy, France.. f.chabot@chu-nancy.fr
SOURCE: Revue des maladies respiratoires, (2006 Dec) Vol. 23, No. 6, pp. 629-41. Ref: 81
Journal code: 8408032. ISSN: 0761-8425.
PUB. COUNTRY: France
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200710
ENTRY DATE: Entered STN: 5 Jan 2007
Last Updated on STN: 25 Oct 2007
Entered Medline: 24 Oct 2007
AB INTRODUCTION: Porto-pulmonary hypertension (PoPH) is the association of pulmonary artery hypertension and portal hypertension. The diagnosis of PoPH is based on pulmonary haemodynamic criteria, obtained via right heart catheterisation, including an increase in mean pulmonary arterial pressure (> 25 mmHg) and in pulmonary vascular resistance (> 240 dyn.s.cm-5). STATE OF THE ART: The exact pathophysiological mechanisms of PoPH are unknown. However, since PoPH has been reported in patients with non-hepatic portal hypertension, the factor that determines the development must be portal hypertension rather than liver disease per se. Moreover, no simple relationship has been identified between the degree of hepatic impairment and the severity of PoPH. The clinical presentation is non-specific with haemodynamic failure occurring at the end stage. As a consequence, screening by annual transthoracic echocardiography is highly recommended in potential liver transplant candidates. Therapy with prostacyclin analogues may partially relieve pulmonary arterial hypertension (PAH). Liver transplantation has an uncertain effect in PoPH and because PoPH is associated with a high perioperative mortality, moderate to severe PoPH remains a contraindication for liver transplantation. PERSPECTIVES AND CONCLUSIONS: Recent advances in the management of PoPH have improved the prognosis. The safety and efficacy of oral endothelin receptor antagonists and oral phosphodiesterase inhibitors is currently under evaluation. A therapeutic approach utilising combinations of drugs should provide better long-term results.

L12 ANSWER 10 OF 20 MEDLINE on STN

ACCESSION NUMBER: 2006444363 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16868809
TITLE: Sildenafil decreased pulmonary arterial pressure but may have exacerbated portal hypertension in a patient with cirrhosis and portopulmonary hypertension.
AUTHOR: Wang Ying-Wen; Lin Han-Chieh; Yang Ying-Ying; Hou Ming-Chih; Lee Shou-Dong
CORPORATE SOURCE: Division of Gastroenterology, Department of Medicine, Taipei Veterans General Hospital and National Yang-Ming University School of Medicine, 201, Section 2, Shih-Pai Road, Taipei, 11217, Taiwan.
SOURCE: Journal of gastroenterology, (2006 Jun) Vol. 41, No. 6, pp. 593-7.
Journal code: 9430794. ISSN: 0944-1174.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200702
ENTRY DATE: Entered STN: 27 Jul 2006
Last Updated on STN: 21 Feb 2007
Entered Medline: 20 Feb 2007
AB Portopulmonary hypertension is a recognized but uncommon complication of cirrhosis. Liver transplantation may be contraindicated in patients with severe portopulmonary hypertension. In order to decrease the pulmonary arterial pressure, intravenous administration of epoprostenol has been shown to provide substantial beneficial results in these patients. Additionally, a recent case report demonstrated that long-term oral administration of sildenafil decreased pulmonary arterial pressure, but its effects on splanchnic hemodynamics were not measured. We report on a patient with cirrhosis and portopulmonary hypertension and the changes in the hemodynamic status after an oral administration of sildenafil. This case report clearly delineates that sildenafil decreases pulmonary arterial pressure but may exacerbate portal hypertension and hyperdynamic circulation in patients with cirrhosis and portopulmonary hypertension.

L12 ANSWER 11 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2006007040 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16393289
TITLE: Effect of vardenafil, an inhibitor of phosphodiesterase-5, on portal haemodynamics in normal and cirrhotic liver -- results of a pilot study.
AUTHOR: Deibert P; Schumacher Y-O; Ruecker G; Opitz O G; Blum H E; Rossle M; Kreisel W
CORPORATE SOURCE: Department of Preventive and Rehabilitative Sports Medicine, University Hospital Freiburg, Freiburg, Germany.
SOURCE: Alimentary pharmacology & therapeutics, (2006 Jan 1) Vol. 23, No. 1, pp. 121-8.
Journal code: 8707234. ISSN: 0269-2813.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200605
ENTRY DATE: Entered STN: 6 Jan 2006
Last Updated on STN: 4 May 2006
Entered Medline: 3 May 2006

AB BACKGROUND: Dysregulation of the cyclic guanosine 3',5' monophosphate-nitric oxide system is in part responsible for portal hypertension in cirrhosis. AIM: To test the effects of inhibitors of phosphodiesterase-5 on portal haemodynamics. METHODS: To 18 healthy subjects and 18 patients with Child A liver cirrhosis, 10 mg of vardenafil, an inhibitor of phosphodiesterase-5, were administered orally. Doppler sonographic measurements of hepatic and splanchnic blood flow, systemic blood pressure and heart rate were recorded before, 1 h after, and 48 h after the application. Vardenafil plasma levels were determined after 1 h. In five patients, invasive registration of free and wedged hepatic vein pressure was performed. RESULTS: Portal venous flow increased in patients from 0.82 +/- 0.30 L/min (mean +/- s.d.) by 26% (CI: 16-37%, P = 0.0004) and in healthy subjects from 0.75 +/- 0.20 L/min (mean +/- s.d.) by 19% (CI: 9-28%; P = 0.0010). Celiac and hepatic artery resistivity indices rose significantly. Systemic blood pressure decreased slightly in patients. The wedged hepatic venous pressure gradient decreased in four of five patients with liver cirrhosis. Vardenafil plasma levels were higher in patients (14 +/- 10 microg/L) than in healthy subjects (9 +/- 6 microg/L; n.s.). CONCLUSIONS: Inhibition of phosphodiesterase-5 increases portal flow and lowers portal pressure by a decrease in sinusoidal resistance and may be a novel therapeutic strategy for portal hypertension.

L12 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1303561 CAPLUS
DOCUMENT NUMBER: 144:285886
TITLE: Bosentan for the treatment of pulmonary arterial hypertension. (II)
AUTHOR(S): Antoniu, Sabina A.
CORPORATE SOURCE: Clinic of Pulmonary Disease, University of Medicine and Pharmacy, Iasi, 700070, Rom.
SOURCE: Therapy (2005), 2(6), 849-852
CODEN: THERCR; ISSN: 1475-0708
PUBLISHER: Future Drugs Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Portopulmonary hypertension is defined as pulmonary arterial hypertension occurring in the presence of portal hypertension. It is classified as a subset of pulmonary arterial hypertension and accordingly it is defined hemodynamically. Portopulmonary hypertension shares the main pathol. features as well as diagnostic approach with other forms of pulmonary arterial hypertension. Several nonpharmacol. and pharmacol. approaches are currently available. Among the pharmacol. approaches prostacycline and its derivs., phosphodiesterase-5 inhibitors such as sildenafil and endothelin receptor antagonists such as bosentan, have been used in portopulmonary hypertension treatment. This is a case series report on the long-term efficacy of bosentan treatment for severe (New York Heart Association functional Class III and IV) portopulmonary hypertension.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2005174518 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15797756
TITLE: Novel use of sildenafil in the treatment of portopulmonary hypertension.
AUTHOR: Chua Roderick; Keogh Anne; Miyashita Masami
CORPORATE SOURCE: St. Vincent's Hospital, Sydney, New South Wales, Australia.

SOURCE: The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation, (2005 Apr) Vol. 24, No. 4, pp. 498-500. Journal code: 9102703. ISSN: 1053-2498.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 6 Apr 2005 Last Updated on STN: 29 Jun 2005 Entered Medline: 28 Jun 2005

AB Portopulmonary hypertension is a poorly understood and uncommon complication of advanced chronic liver disease. Current therapy is based largely on treatment options proven in idiopathic pulmonary hypertension. The severity of the portopulmonary hypertension should best be attenuated medically before attempting combined liver and lung transplantation to avoid increased peri-operative mortality. This case report describes the successful use of sildenafil to decrease the pulmonary vascular resistance in a patient with hepatitis-C cirrhosis who was preparing for liver transplantation.

L12 ANSWER 14 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2005078879 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15708146
TITLE: Fatal variceal rupture after sildenafil use: report of a case.
AUTHOR: Finley David S; Lugo Brian; Ridgway James; Teng Wang; Imagawa David K
CORPORATE SOURCE: Division of Hepatobiliary and Pancreas Surgery, Department of Surgery, University of California, Irvine, Orange, California 92868, USA.. finds@uci.edu
SOURCE: Current surgery, (2005 Jan-Feb) Vol. 62, No. 1, pp. 55-6. Journal code: 7802123. ISSN: 0149-7944.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 16 Feb 2005 Last Updated on STN: 24 Jun 2005 Entered Medline: 23 Jun 2005

AB Sildenafil may increase the risk of variceal bleeding in portal hyptertension by increasing splanchnic blood flow. We report herein the second case of variceal rupture after sildenafil use.

L12 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:1080763 CAPLUS
DOCUMENT NUMBER: 142:16820
TITLE: Use of a phosphodiesterase V inhibitor for the prophylaxis and/or treatment of portal hypertension
INVENTOR(S): Kreisel, Wolfgang
PATENT ASSIGNEE(S): Universitatsklinikum Freiburg, Germany
SOURCE: PCT Int. Appl., 32 pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108062	A2	20041216	WO 2004-EP6014	20040603
WO 2004108062	A3	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10325813	A1	20050105	DE 2003-10325813	20030606
DE 10325813	B4	20071220		
EP 1635838	A2	20060322	EP 2004-739573	20040603
EP 1635838	B1	20070502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1871010	A	20061129	CN 2004-80022512	20040603
JP 2006527177	T	20061130	JP 2006-508268	20040603
AT 361074	T	20070515	AT 2004-739573	20040603
ES 2287740	T3	20071216	ES 2004-739573	20040603
EP 1923073	A2	20080521	EP 2006-25229	20040603
EP 1923073	A3	20080709		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 20070004744	A1	20070104	US 2006-559694	20060501

PRIORITY APPLN. INFO.:			
DE 2003-10325813	A	20030606	
EP 2004-739573	A3	20040603	
WO 2004-EP6014	W	20040603	

AB The invention discloses a medicament for the prophylaxis and/or treatment of diseases or complications associated with portal hypertension, especially hemorrhagic complications. The invention uses a phosphodiesterase V inhibitor, e.g. sildenafil.

L12 ANSWER 16 OF 20 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004205321 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15102002
TITLE: Systemic and splanchnic haemodynamic effects of sildenafil in an in vivo animal model of cirrhosis support for a risk in cirrhotic patients.
AUTHOR: Colle Isabelle; De Vriese An S; Van Vlierberghe Hans; Lameire Norbert H; DeVos Martine
CORPORATE SOURCE: Department of Medicine, Ghent University Hospital, Ghent, Belgium.. Isabelle.Colle@rug.ac.be
SOURCE: Liver international : official journal of the International Association for the Study of the Liver, (2004 Feb) Vol. 24, No. 1, pp. 63-8.
Journal code: 101160857. ISSN: 1478-3223.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 23 Apr 2004

Last Updated on STN: 28 May 2004
Entered Medline: 27 May 2004

AB OBJECTIVES: Sildenafil is a selective inhibitor of the cGMP-specific phosphodiesterase type V (PDE-V) in the corpus cavernosum. PDE-V is also present in the mesenteric artery. Cirrhosis is complicated by a splanchnic vasodilation attributed to a local overproduction of nitric oxide (NO). As sildenafil potentiates the effects of NO, it may further decrease mesenteric vascular tone and increase portal venous blood flow. The aim is to evaluate the effects of sildenafil on the systemic and splanchnic haemodynamics in an experimental model of cirrhosis. METHODS: Secondary biliary cirrhosis was induced in male Wistar rats by common bile duct ligation (CBDL, n=8); control rats were sham-operated (sham, n=7). The mean arterial pressure (MAP), portal venous pressure (PVP) and arterial mesenteric blood flow (MBF) were measured after intramesenteric (0.01-10 mg/kg) and after intravenous (i.v.) (0.01-10 mg/kg) administration of sildenafil. RESULTS: Baseline PVP was significantly higher in CBDL than in sham rats, whereas baseline MAP tended to be lower and MBF tended to be higher in CBDL compared with sham rats. Both intramesenteric and i.v. injection of sildenafil significantly decreased MAP and increased MBF and PVP in a dose-dependent way. The decrease in MAP was significantly less important in CBDL than in sham rats. The increase in MBF was importantly lower in CBDL than in sham rats. PVP tended to increase more significantly in sham rats than in CBDL. CONCLUSION: Sildenafil increases MBF and PVP and induces systemic hypotension. The effects are less pronounced in cirrhosis, suggesting vascular hyporesponsiveness to sildenafil. Although the rise in PVP in cirrhotic animals is smaller than in controls, it may present a risk for haemorrhagic complications. Further studies are necessary before prescribing sildenafil to patients with cirrhosis.

L12 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:590998 CAPLUS
DOCUMENT NUMBER: 139:128037
TITLE: Use of acetylcholine esterase antagonists to treat insulin resistance
INVENTOR(S): Lautt, Wayne W.
PATENT ASSIGNEE(S): Diamedica Inc., Can.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061648	A1	20030731	WO 2003-CA78	20030127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20030235609	A1	20031225	US 2003-350478	20030124
CA 2514088	A1	20030731	CA 2003-2514088	20030127
EP 1471905	A1	20041103	EP 2003-700275	20030127

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2005519906	T	20050707	JP 2003-561592		20030127
AU 2003201578	B2	20080306	AU 2003-201578		20030127
US 20050049293	A1	20050303	US 2004-502066		20041027
PRIORITY APPLN. INFO.:			US 2002-350958P	P	20020125
			WO 2003-CA78	W	20030127

AB A method is provided for reducing insulin resistance in a mammalian subject, comprising administering a suitable acetylcholine esterase antagonist.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 20 MEDLINE on STN

ACCESSION NUMBER: 2003524976 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14603504
TITLE: Pharmacokinetics of DA-8159, a new erectogenic, after intravenous and oral administration to rats: hepatic and intestinal first-pass effects.
AUTHOR: Shim Hyun J; Kim Yu C; Park Kyung J; Kim Dong S; Kwon Jong W; Kim Won B; Lee Myung G
CORPORATE SOURCE: College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul, South Korea.
SOURCE: Journal of pharmaceutical sciences, (2003 Nov) Vol. 92, No. 11, pp. 2185-95.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 7 Nov 2003
Last Updated on STN: 24 Jun 2004
Entered Medline: 18 Jun 2004

AB The purposes of this study were to report dose-independent (after intravenous administration) and dose-dependent (after oral administration) area under the curve of plasma concentration versus time from time zero to time infinity (AUC), and gastric, intestinal, and/or hepatic first-pass effects (after intravenous, intraportal, intragastric, and intraduodenal administration) of DA-8159 [5-[2-propyloxy-5-(1-methyl-2-pyrollidinylethylamidosulfonyl)phenyl]-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo(4,3-d)pyrimidine-7-one], a new erectogenic, in rats. After intravenous administration at doses of 5, 10, and 30 mg/kg, the AUCs and time-averaged total body clearances (CLs) were dose-independent. However, the AUCs were dose-dependent after oral administration at doses of 20, 30, 50, and 100 mg/kg. This result could be due to saturation of first-pass effects at high doses. The extent of absolute oral bioavailability (F) of DA-8159 was 38.0% at a dose of 30 mg/kg. Considering almost complete absorption of DA-8159 from rat gastrointestinal tract (approximately 99% of oral dose of 30 mg/kg), the low F could be due to considerable hepatic, gastric, and/or intestinal first-pass effects. After intravenous administration at three doses, the CLs were considerably slower than the reported cardiac output in rats, suggesting almost negligible first-pass effect of DA-8159 in the heart and lung. The AUCs were not significantly different between intragastric and intraduodenal administration of DA-8159 at a dose of 30 mg/kg (131 and 127 microg x min/mL), suggesting that gastric first-pass effect of DA-8159 was almost negligible in rats. However, the values were significantly smaller than that after intraportal administration (311 microg x min/mL), indicating considerable intestinal

first-pass effect of DA-8159 in rats of approximately 58% of the oral dose. Approximately 23% of DA-8159 at a dose of 30 mg/kg absorbed into the portal vein was eliminated by the liver (hepatic first-pass effect) based on AUC difference between intravenous and intraportal administration (the value, 23%, was equivalent to approximately 9.6% of oral dose). The low F of DA-8159 after oral administration at a dose of 30 mg/kg to rats was mainly due to considerable intestinal (approximately 58%) first-pass effects.
 J Pharm Sci 92:2185-2195, 2003

L12 ANSWER 19 OF 20 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005074182 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15703602
TITLE: Gastroduodenal motility.
AUTHOR: Ramkumar Davendra; Schulze Konrad S
CORPORATE SOURCE: University of Iowa HealthCare and VAMC, Iowa City, Iowa, USA.. davendra_ramkumar@uiowa.edu
SOURCE: Current opinion in gastroenterology, (2003 Nov) Vol. 19, No. 6, pp. 540-5.
Journal code: 8506887. ISSN: 0267-1379.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; PUBMED-NOT-MEDLINE
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 11 Feb 2005
Last Updated on STN: 29 Mar 2005
Entered Medline: 28 Mar 2005
AB PURPOSE OF REVIEW: The neuromuscular function of the stomach and duodenum provides the mechanical forces that drive digestion and are responsible for sensations of satiety and of dyspepsia. This article reviews (1) the neuroendocrine factors controlling upper gastrointestinal motility, (2) noninvasive techniques to evaluate gastroduodenal motility, and (3) the pathophysiology and treatment of gastroparesis. RECENT FINDINGS: Nutrients in the duodenum inhibit gastric emptying via a feedback pathway that involves release of cholecystokinin and serotonin (5-HT) from neuroendocrine cells; both act peripherally, cholecystokinin via cholecystokinin A receptors and serotonin via 5-HT3 receptors. The dorsal vagal complex plays a central role in the gastric inhibition mediated by tumor necrosis factor-alpha. The construction of maps that define intestinal movements in time and space has now been extended to the stomach. MRI compares favorably with the barostat in assessing gastric volume accommodation to meals and drugs and has the advantage of being noninvasive and showing contractions. Gastroparesis is increasingly recognized as a complication of end-stage liver disease; ascites plays no role in this, but portal hypertension stiffens the gastric walls and creates hypoxic conditions that may interfere with the neuromuscular functions of the stomach. Promising for the treatment of gastroparesis are clonidine, sildenafil, and intrapyloric botulinum toxin. Electrical stimulation triggers a vagally mediated relaxation of the stomach. SUMMARY: Drugs may be designed that specifically act on 5-HT3, cholecystokinin, or TNF-alpha receptors. Spatiotemporal maps should boost the diagnostic yield from dynamic imaging of motility using ultrasound, computed axial tomography scan, or MRI and the understanding of the mechanical forces driving digestion. Symptomatic benefit in gastroparesis may derive more from improved accommodation than gastric emptying.

L12 ANSWER 20 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2001662941 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11708765

TITLE: Current management of primary pulmonary hypertension.
AUTHOR: Klings E S; Farber H W
CORPORATE SOURCE: The Pulmonary Center, Boston University School of Medicine, Massachusetts 02118, USA.. eklings@lung.bumc.bu.edu
SOURCE: Drugs, (2001) Vol. 61, No. 13, pp. 1945-56. Ref: 59
Journal code: 7600076. ISSN: 0012-6667.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 19 Nov 2001
Last Updated on STN: 8 Mar 2002
Entered Medline: 7 Mar 2002

AB Primary pulmonary hypertension (PPH) is a rare disorder with an annual incidence of 1 to 2 per million people. The aetiology of this disorder is unknown, but it appears to result from an abnormal interaction of environmental and genetic factors leading to a vasculopathy. The pulmonary arteries in these patients exhibit a spectrum of pathological lesions ranging from the early medial hypertrophy to the end-stage fibrotic plexiform lesions. This characteristic pathology is also observed in pulmonary hypertension resulting from connective tissue disease (particularly systemic sclerosis), HIV infection, portal hypertension and certain toxins. PPH is a condition that is difficult to diagnose and treat, with a median survival of 2.8 years in historical studies. One of the difficulties in treating patients with PHH is that the subacute nature of disease presentation often prevents an accurate diagnosis during the early stages of the illness. Progressive dyspnoea on exertion is the most common presenting symptom. Diagnostic evaluation should include electrocardiography, chest radiograph and echocardiography, and laboratory and other studies to evaluate for secondary causes (e.g. pulmonary function tests, chest computed tomography and ventilation/perfusion scans, pulmonary arteriogram, cardiopulmonary testing, right heart catherisation). PHH is a disorder for which there is no known cure. Current medical and surgical treatment options for patients with PHH include anticoagulation, vasodilators and transplantation. Calcium channel antagonists are currently the oral drugs of choice for the treatment of patients with New York Heart Association (NYHA) Class II disease. These agents, in particular the dihydropyridine compounds, have beneficial effects on haemodynamics and right ventricular function, and possibly increased survival. Epoprostenol is administered by intravenous infusion, and studies have demonstrated short- and long-term improvements in symptoms, haemodynamics and survival. It is well tolerated and has become the treatment of choice for patients with NYHA Class III and IV disease. Inotropic agents are used as a bridge to transplant, which is indicated in patients who do not respond to maximal medical therapy. Experience has shown that single lung, double lung and heart-lung transplantation are approximately of equal efficacy. Currently, single lung transplant appears to be the procedure of choice. Newer agents, such as sildenafil, beraprost and bosentan, are presently being evaluated for the treatment of this disorder. Future study should include elucidation of the pathogenic mechanisms in the development of this vasculopathy, which will hopefully lead to the development of improved treatment options for patients with PHH.

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=> s inflammatory pain
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=> s l1 and prevention
L2         238 L1 AND PREVENTION

=> s l1 (s) prevention
L3          87 L1 (S) PREVENTION

=> s l3 and rev/dt
L4           0 L3 AND REV/DT

=> d scan l3

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CC   27-14 (Heterocyclic Compounds (One Hetero Atom))
     Section cross-reference(s): 1, 63
TI   Chromenones and their use as modulators of metabotropic glutamate
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receptors, preparation, pharmaceutical compositions and use in the treatment of neurological disorders

ST chromenone prepn metabotropic glutamate receptor modulator treatment neurol disorder

IT Obesity
(-related disorders, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT AIDS (disease)
Dementia
(AIDS dementia complex, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Brain, disease
Prion diseases
(Creutzfeldt-Jakob, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Nervous system, disease
Nervous system, disease
(Huntington's chorea, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Nervous system, disease
Pain
(acute, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Mental and behavioral disorders
(agoraphobia, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Pain
Skin, disease
(allodynia, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Mental and behavioral disorders
(attention deficit hyperactivity disorder, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Mental and behavioral disorders
(autism, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Eating disorders
(binge, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Mental and behavioral disorders
(bipolar disorder, manic-depressive, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Pain
(cancer, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Injury
(cerebral, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Development, mammalian postnatal

(child; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Nervous system, disease
(chorea, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Laryngitis
Nervous system, disease
Pain
(chronic, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Pharmaceutical tablets
(coated tablets; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Mental and behavioral disorders
(delirium, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Mental and behavioral disorders
(delusional, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Mental and behavioral disorders
(dementia pugilistica, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Viral infection
(depression resulting from Borna virus, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Borna disease virus
(depression resulting from, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Mental and behavioral disorders
(depression, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Mitochondria
(disease, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Micturition
(disorders, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Tinnitus
(drug-induced, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Nervous system, disease
(dyskinesia, L-Dopa-induced, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Nervous system, disease
(dystonia, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Dementia

(frontal lobe, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Digestive tract, disease
(functional, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Digestive tract, disease
(gastroesophageal reflux, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Anxiety
(generalized, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Neurotransmission
(glutamatergic; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Injury
(head and neck, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Brain, disease
(hepatic encephalopathy, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Pain
(hyperalgesia, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Hyperkinesia
(in children, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Neuromuscular diseases
(in lower urinary tract, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Respiratory system, disease
(infection, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Prion diseases
(infectious, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Pain
(inflammatory pain, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Pharmaceutical injections
Pharmaceutical solutions
(injectable solns.; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Brain, disease
Eye, disease
Head and Neck, disease
Spinal cord, disease
(injury, treatment of; preparation of chromenones as metabotropic glutamate

receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Ear
(inner, disease, insult, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Intestine, disease
(irritable bowel syndrome, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Cardiac arrest
(ischemia resulting from, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Metabotropic glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mGluR5; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Retinal disease
(macular degeneration, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Brain, disease
Prion diseases
(mad cow, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Mental and behavioral disorders
(major depression, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Headache
(migraine, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Cognitive disorders
(mild, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Disease, animal
(mitochondrial, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Nerve, disease
(motor, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Urinary system, disease
(neuromuscular lower, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Pain
(neuropathic pain, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Pain
(nociceptive, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Mental and behavioral disorders
(obsession-compulsion, treatment of; preparation of chromenones as

metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Injury
(ocular, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Oral drug delivery systems
Pharmaceutical liquids
(oral liqs.; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Rheumatoid arthritis
(pain related to, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Hypoxia
(perinatal, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Schizophrenia
(pos. or cognitive or neg. symptoms of, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Cognitive disorders
(post-operative, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Mental and behavioral disorders
(post-traumatic stress disorder, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Analgesics
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-infective agents
Anti-ischemic agents
Antiasthmatics
Anticonvulsants
Antidepressants
Antiglaucoma agents
Antimigraine agents
Antiobesity agents
Antiparkinsonian agents
Antipsychotics
Antitumor agents
Antiviral agents
Anxiolytics
Astrocyte
Cognition enhancers
Coronary bypass surgery
Drug tolerance
Gastrointestinal agents
Human
Immunosuppressants
Muscle relaxants
Nervous system agents
Neuroprotective agents
Pharmaceutical aerosols
Pharmaceutical capsules
Pharmaceutical excipients
Pharmaceutical tablets
Prophylaxis

Transplant and Transplantation
(preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Opioids
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Metabotropic glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Mental and behavioral disorders
(psychosis, substance-induced, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Asthma
(reflux-related, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Leg, disease
Sleep disorders
(restless leg syndrome, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Mental and behavioral disorders
(schizoaffective disorder, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Mental and behavioral disorders
(schizophreniform, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Anxiety
(social, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Tinnitus
(sound-induced, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Muscle, disease
(spasm, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Nervous system, disease
(spasticity, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Esophagus
(sphincter, gastroesophageal, disease, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Injury
(spinal cord, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Nervous system, disease
(spinocerebellar ataxia, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the

prevention and treatment acute and/or chronic neurol. disorders)

IT Anxiety
(substance-induced, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Nervous system, disease
(tardive dyskinesia, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Epilepsy
(temporal lobe, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Injury
(trauma, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Alcoholism
Alzheimer's disease
Alzheimer's disease
Amyotrophic lateral sclerosis
Anxiety
Asthma
Bulimia
Cognitive disorders
Convulsion
Dementia
Down's syndrome
Drug dependence
Drug dependence
Dyspepsia
Eating disorders
Epilepsy
Eye, disease
Fragile X syndrome
Glaucoma
Hypoglycemia
Hypoxia
Ischemia
Lung, disease
Mitral valve insufficiency
Movement disorders
Multiple sclerosis
Multiple sclerosis
Neoplasm
Neuroglia, neoplasm
Obesity
Pain
Parkinson's disease
Pruritus
Retinal disease
Schizophrenia
Sleep disorders
Stroke
Substance abuse
Tinnitus
Tinnitus
Tobacco smoke
Wernicke-Korsakoff syndrome
(treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT Dementia
(vascular, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Transferrins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(τ-transferrins, - related disease, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT Amyloid
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(β-, - related disease, treatment of; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT 1035637-33-2 1044918-30-0 1044918-31-1 1044918-32-2 1044918-33-3
1044918-34-4 1044918-42-4
RL: PRPH (Prophetic)
(Chromenones and their use as modulators of metabotropic glutamate receptors, preparation, pharmaceutical compositions and use in the treatment of neurological disorders)
IT 934966-12-8P 934966-13-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate and intermediate; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)
IT 64267-25-0P 300839-05-8P 301196-68-9P 304894-66-4P 306321-91-5P
306321-92-6P 307550-27-2P 313471-07-7P 325737-67-5P 325822-09-1P
328022-10-2P 335419-13-1P 380476-01-7P 887698-18-2P 934966-01-5P
934966-02-6P 934966-03-7P 934966-04-8P 934966-05-9P 934966-06-0P
934966-07-1P 934966-08-2P 934966-09-3P 934966-10-6P 934966-11-7P
934966-14-0P 934966-15-1P 934966-17-3P 934966-18-4P 934966-19-5P
934966-20-8P 934966-21-9P 934966-22-0P 934966-23-1P 934966-24-2P
934966-25-3P 934966-26-4P 934966-27-5P 934966-28-6P 934966-29-7P
934966-30-0P 934966-31-1P 934966-32-2P 934966-33-3P 934966-34-4P
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934966-45-7P 934966-46-8P 934966-47-9P 934966-48-0P 934966-49-1P
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934966-55-9P 934966-56-0P 934966-58-2P 934966-60-6P 934966-61-7P
934966-63-9P 934966-65-1P 934966-67-3P 934966-68-4P 934966-70-8P
934966-72-0P 934966-74-2P 934966-76-4P 934966-78-6P 934966-80-0P
934966-82-2P 934966-84-4P 934966-86-6P 934966-88-8P 934966-90-2P
934966-92-4P 934966-93-5P 934966-94-6P 934966-95-7P 934966-96-8P
934966-97-9P 934966-98-0P 934966-99-1P 934967-00-7P 934967-01-8P
934967-02-9P 934967-03-0P 934967-04-1P 934967-05-2P 934967-06-3P
934967-07-4P 934967-08-5P 934967-09-6P 934967-10-9P 934967-11-0P
934967-12-1P 934967-13-2P 934967-14-3P 934967-15-4P 934967-16-5P
934967-17-6P 934967-18-7P 934967-19-8P 934967-20-1P 934967-21-2P
934967-22-3P 934967-23-4P 934967-24-5P 934967-25-6P 934967-26-7P
934967-27-8P 934967-28-9P 934967-29-0P 934967-30-3P 934967-31-4P
934967-32-5P 934967-34-7P 934967-35-8P 934967-36-9P 934967-37-0P
934967-38-1P 934967-39-2P 934967-40-5P 934967-41-6P 934967-42-7P
934967-43-8P 934967-44-9P 934967-45-0P 934967-46-1P 934967-47-2P
934967-48-3P 934967-49-4P 934967-50-7P 934967-51-8P 934967-52-9P
934967-53-0P 934967-54-1P 934967-55-2P 934967-56-3P 934967-57-4P
934967-58-5P 934967-59-6P 934967-60-9P 934967-61-0P 934967-62-1P
934967-63-2P 934967-64-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT 3722-44-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT 50-36-2, Cocaine 54-11-5, Nicotine 59-92-7, biological studies 300-62-9, Amphetamine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT 56-86-0, L-Glutamic acid, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

IT 75-26-3, 2-Bromopropane 108-46-3, Resorcinol, reactions 1655-07-8, Ethyl 2-oxocyclohexanecarboxylate
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of chromenones as metabotropic glutamate receptor modulators and their use in the prevention and treatment acute and/or chronic neurol. disorders)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 87 ANSWERS CAPLUS COPYRIGHT 2008 ACS on STN

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

TI Preparation of novel 2-aminopyridine derivatives as potassium channel modulators

ST aminopyridine prepn small conductance calcium activated potassium channel modulator; pyridinamine prepn small conductance calcium activated potassium channel modulator

IT Amnesia
(age-related; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Nervous system, disease
(ataxia; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Mental and behavioral disorders
(attention deficit disorder; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Mental and behavioral disorders
(bipolar disorder; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Bladder, disease
(bladder hyperexcitability; preparation of novel 2-aminopyridine derivs. as

modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Bladder, disease
(bladder spasms; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Ischemia
(cerebral; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Intestine, disease
(constipation; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Mental and behavioral disorders
(depression; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Gastrointestinal motility
(disorder, dysmotility, hypomotility; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Gastrointestinal motility
(disorder, dysmotility; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Digestive tract, disease
(gastroesophageal reflux; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Intestine, disease
(ileus; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Sexual disorders
(impotence, male; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Bladder, disease
(incontinence; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Pain
(inflammatory pain; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Calcium-activated potassium channels
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(intermediate and small conductance; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Intestine, disease
(irritable bowel syndrome; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Brain, disease
(ischemia; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Memory disorders
(memory retention defect; preparation of novel 2-aminopyridine derivs. as

modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Headache
(migraine; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Mental and behavioral disorders
(mood-affecting; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Nerve, disease
(motor; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Disease, animal
(myokymia; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Muscular dystrophy
(myotonic; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Pain
(neuropathic pain; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Diabetes mellitus
(non-insulin-dependent; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Bladder, disease
(obstruction; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Epilepsy
(petit mal; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Kidney, disease
(polycystic; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Parturition disorders
(premature parturition; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)
IT Aging, animal
Alopecia
Alzheimer's disease
Analgesics
Angina pectoris
Anti-Alzheimer's agents
Anti-inflammatory agents
Anti-ischemic agents
Antianginal agents
Antiarrhythmics
Antiasthmatics
Anticonvulsants
Antidepressants
Antidiabetic agents
Antidiarrheals
Antifibrotic agents

Antihypertensives
Antimigraine agents
Antiparkinsonian agents
Antipsychotics
Antitumor agents
Anxiety
Anxiolytics
Asthma
Brain, neoplasm
Cardiac arrhythmia
Cardiovascular agents
Cardiovascular system, disease
Chronic obstructive pulmonary disease
Cognition enhancers
Cognitive disorders
Colitis
Convulsion
Coronary artery disease
Coronary spasm
Cystic fibrosis
Dementia
Digestive tract, disease
Dysmenorrhea
Epilepsy
Gastrointestinal agents
Hearing loss
Human
Hypertension
Immunostimulants
Immunosuppression
Inflammatory bowel disease
Intermittent claudication
Ischemia
Kidney, disease
Laxatives
Learning disorders
Myocardial ischemia
Narcolepsy
Neoplasm
Nervous system agents
Pain
Parkinson's disease
Pharmaceutical carriers
Pharmaceutical excipients
Prophylaxis
Raynaud disease
Respiratory system agents
Seizures
Sjogren syndrome
Sleep apnea
Sleep disorders
Stroke
Tocolytic agents
Urogenital system, disease
(preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Mental and behavioral disorders
(psychosis; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Disease, animal

(responsive to modulation of SK channels; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Nose, disease
(rhinorrhea; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Diarrhea
(secretory; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Blood vessel, disease
(spasm; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Muscle relaxants
(spasmolytics; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Nervous system, disease
(spasticity; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Brain, disease
(trauma; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Nerve, disease
Pain
(trigeminal neuralgia; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Vision disorders
(vision loss; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT Mouth, disease
(xerostomia; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT 9004-10-8, Insulin, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(hyperinsulinemia; preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT 1026776-13-5P 1026776-14-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT 138563-55-0P 666258-99-7P 1026776-15-7P 1026776-16-8P
RL: PRPH (Prophetic); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

IT 372-48-5, 2-Fluoropyridine 3863-11-4, 3,4-Difluoroaniline 72235-53-1, 3,4-Difluorobenzylamine 85118-01-0, 3,4-Difluorobenzyl bromide

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of novel 2-aminopyridine derivs. as modulators of small-conductance calcium-activated potassium channels useful in treatment and prevention of diseases)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> s inflammatory pain and rev/dt
L5 0 INFLAMMATORY PAIN AND REV/DT

=> s inflammatory pain/ti
L6 706 INFLAMMATORY PAIN/TI

=> s l6 and trpv3
L7 0 L6 AND TRPV3

=> s trpv3
L8 201 TRPV3

=> s l8 and pain
L9 52 L8 AND PAIN

=> d l9 ibib abs 1-52

L9 ANSWER 1 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:621215 CAPLUS
DOCUMENT NUMBER: 149:171764
TITLE: Citral sensing by TRANSient receptor potential channels in dorsal root ganglion neurons
AUTHOR(S): Stotz, Stephanie C.; Vriens, Joris; Martyn, Derek; Clardy, Jon; Clapham, David E.
CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Cardiology, Children's Hospital, Boston, MA, USA
SOURCE: PLoS One (2008), 3(5), No pp. given
CODEN: POLNCL; ISSN: 1932-6203
URL: http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0002082
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Transient receptor potential (TRP) ion channels mediate key aspects of taste, smell, pain, temperature sensation, and pheromone detection. To deepen our understanding of TRP channel physiol., we require more diverse pharmacol. tools. Citral, a bioactive component of lemongrass, is commonly used as a taste enhancer, as an odorant in perfumes, and as an insect repellent. Here we report that citral activates TRP channels found in sensory neurons (TRPV1 and TRPV3, TRPM8, and TRPA1), and produces long-lasting inhibition of TRPV1-3 and TRPM8, while transiently blocking TRPV4 and TRPA1. Sustained citral inhibition is independent of internal calcium concentration, but is state-dependent, developing only after TRP channel opening. Citral's actions as a partial agonist are not due to cysteine modification of the channels nor are they a consequence of citral's stereoisoforms. The isolated aldehyde and alc. cis and trans enantiomers (neral, nerol, geranial, and geraniol) each reproduce citral's actions. In juvenile rat dorsal root ganglion neurons, prolonged citral inhibition of native TRPV1 channels enabled the separation of TRPV2 and TRPV3 currents. We find that TRPV2 and TRPV3 channels are present in a high proportion of these neurons (94% respond to 2-aminoethyldiphenyl borate), consistent with our immunolabeling expts. and previous in situ hybridization studies. The TRPV1 activation requires residues in transmembrane segments two through four of the voltage-sensor

domain, a region previously implicated in capsaicin activation of TRPV1 and analogous menthol activation of TRPM8. Citral's broad spectrum and prolonged sensory inhibition may prove more useful than capsaicin for allodynia, itch, or other types of pain involving superficial sensory nerves and skin.
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:573286 CAPLUS
DOCUMENT NUMBER: 149:49726
TITLE: ThermoTRP channels in nociceptors: taking a lead from capsaicin receptor TRPV1
AUTHOR(S): Mandadi, Sravan; Roufogalis, Basil D.
CORPORATE SOURCE: Hotchkiss Brain Institute, Calgary, AB, T2N 4N1, Can.
SOURCE: Current Neuropharmacology (2008), 6(1), 21-38
CODEN: CNUEAN; ISSN: 1875-6190
URL: http://www.ingentaconnect.com/content/ben/cn/2008/00000006/00000001
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Nociceptors with peripheral and central projections express temperature sensitive transient receptor potential (TRP) ion channels, also called thermoTRP's. Chemosensitivity of thermoTRP's to certain natural compds. eliciting pain or exhibiting thermal properties has proven to be a good tool in characterizing these receptors. Capsaicin, a pungent chemical in hot peppers, has assisted in the cloning of the first thermoTRP, TRPV1. This discovery initiated the search for other receptors encoding the response to a wide range of temps. encountered by the body. Of these, TRPV1 and TRPV2 encode unique modalities of thermal pain when exposed to noxious heat. The ability of TRPA1 to encode noxious cold is presently being debated. The role of TRPV1 in peripheral inflammatory pain and central sensitization during chronic pain is well known. In addition to endogenous agonists, a wide variety of chemical agonists and antagonists have been discovered to activate and inhibit TRPV1. Efforts are underway to determine conditions under which agonist-mediated desensitization of TRPV1 or inhibition by antagonists can produce analgesia. Also, identification of specific second messenger mols. that regulate phosphorylation of TRPV1 has been the focus of intense research, to exploit a broader approach to pain treatment. The search for a role of TRPV2 in pain remains dormant due to the lack of suitable exptl. models. However, progress into TRPA1's role in pain has received much attention recently. Another thermoTRP, TRPM8, encoding for the cool sensation and also expressed in nociceptors, has recently been shown to reduce pain via a central mechanism, thus opening a novel strategy for achieving analgesia. The role of other thermoTRP's (TRPV3 and TRPV4) encoding for detection of warm temps. and expressed in nociceptors cannot be excluded. This review will discuss current knowledge on the role of nociceptor thermoTRPs in pain and therapy and describes the activator and inhibitor mols. known to interact with them and modulate their activity.
REFERENCE COUNT: 247 THERE ARE 247 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:543349 CAPLUS
DOCUMENT NUMBER: 148:464924
TITLE: TRP channels and nociception
AUTHOR(S): Tominaga, Makoto
CORPORATE SOURCE: Section of Cell Signaling, Okazaki Institute for

Integrative Bioscience, National Institutes of Natural Sciences, Okazaki, 444-8787, Japan

SOURCE: Cellular and Molecular Mechanisms for the Modulation of Nociceptive Transmission in the Peripheral and Central Nervous Systems (2007), 23-40. Editor(s): Kumamoto, Eiichi. Research Signpost: Trivandrum, India.
CODEN: 69KOVE; ISBN: 81-308-0162-0

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review. Pain is initiated when noxious stimuli excite the peripheral terminals of specialized primary afferent neurons called nociceptors. A lot of mols. are involved in conversion of the noxious stimuli to the elec. signals in the nociceptor endings. Among them, TRP channels play important roles in detecting the noxious stimuli including chemical and thermal ones.

REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:353105 CAPLUS

DOCUMENT NUMBER: 148:369982

TITLE: Dihydroquinoline compounds for modulating calcium channel TRPV3 function, and use for the treatment of pain

INVENTOR(S): Mogan, Magdalene M.; Chong, Jayhong A.; Fanger, Christopher; Ripka, Amy; Larsen, Glenn R.; Zhen, Xiaoguang; Underwood, Dennis John; Weigele, Manfred

PATENT ASSIGNEE(S): Hydra Biosciences Inc., USA

SOURCE: PCT Int. Appl., 130pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2008033564	A1	20080320	WO 2007-US20195		20070914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080146611	A1	20080619	US 2007-901253		20070914
PRIORITY APPLN. INFO.:			US 2006-845039P	P	20060915
			US 2006-859139P	P	20061115

OTHER SOURCE(S): MARPAT 148:369982

AB The application discloses compds. and methods for treating pain and other conditions related to TRPV3 using dihydroquinoline derivative TRPV channel inhibitors. Compound preparation is included.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:271658 CAPLUS
DOCUMENT NUMBER: 148:535310
TITLE: Investigation of TRPV1 loss-of-function phenotypes in transgenic shRNA expressing and knockout mice
AUTHOR(S): Christoph, Thomas; Bahrenberg, Gregor; De Vry, Jean; Englberger, Werner; Erdmann, Volker A.; Frech, Moritz; Koegel, Babette; Roehl, Thomas; Schiene, Klaus; Schroeder, Wolfgang; Seibler, Jost; Kurreck, Jens
CORPORATE SOURCE: Preclinical Research and Development, Department of Pharmacology, Gruenenthal, Aachen, 52078, Germany
SOURCE: Molecular and Cellular Neuroscience (2008), 37(3), 579-589
CODEN: MOCNED; ISSN: 1044-7431
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The function of the transient receptor potential vanilloid 1 (TRPV1) cation channel was analyzed with RNA interference technologies and compared to TRPV1 knockout mice. Expression of shRNAs targeting TRPV1 in transgenic (tg) mice was proven by RNase protection assays, and TRPV1 downregulation was confirmed by reduced expression of TRPV1 mRNA and lack of receptor agonist binding in spinal cord membranes. Unexpectedly, TRPV3 mRNA expression was upregulated in shRNAtg but downregulated in knockout mice. Capsaicin-induced [Ca2+]i changes in small diameter DRG neurons were significantly diminished in TRPV1 shRNAtg mice, and administration of capsaicin hardly induced hypothermia or nocifensive behavior in vivo. Likewise, sensitivity towards noxious heat was reduced. Interestingly, spinal nerve injured TRPV1 knockout but not shRNAtg animals developed mech. allodynia and hypersensitivity. The present study provides further evidence for the relevance of TRPV1 in neuropathic pain and characterizes RNA interference as valuable technique for drug target validation in pain research.
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:208631 CAPLUS
DOCUMENT NUMBER: 148:304671
TITLE: TRP channels and nociception
AUTHOR(S): Tominaga, Makoto
CORPORATE SOURCE: Okazaki Institute fro Integrative Bioscience, National Institute of Natural Sciences, Aichi, Japan
SOURCE: Igaku no Ayumi (2007), 223(9), 663-667
CODEN: IGAYAY; ISSN: 0039-2359
PUBLISHER: Ishiyaku Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review discussing (1) capsaicin receptor TRPV1, (2) TRPV2 as TRP channel, (3) cold-Menthol-Receptor TRPM8, (4) TRPA1 and (5) TRPV3 and TRPV4.

L9 ANSWER 7 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1177636 CAPLUS
DOCUMENT NUMBER: 147:469238
TITLE: Fused piperidine derivatives as modulators of gated ion channels, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Demnitz, Joachim; Ahring, Philip K.
PATENT ASSIGNEE(S): Painceptor Pharma Corporation, Can.
SOURCE: PCT Int. Appl., 100pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007115403	A1	20071018	WO 2007-CA580	20070410

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 20080021034	A1	20080124	US 2007-786420	20070410

PRIORITY APPLN. INFO.: US 2006-791125P P 20060410
OTHER SOURCE(S): MARPAT 147:469238
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to fused piperidine derivs. of formula I or II, which are modulators of gated ion channels. In compds. I, the dotted bonds represent a single bond or double bond; X and Y are independently selected from N, C, and CH; R1 is selected from H, C1-4 alkyl, Ph, phenyl-C1-4 alkyl, C1-4 alkoxy-C1-4 alkyl, C1-4 alkylsulfonyl, etc.; R2 is absent, H, cyano, nitro, amino, CO2H, C1-4 alkoxycarbonyl, (un)substituted carbamoyl, and (un)substituted ureido; R3 is H, C1-4 alkyl, C1-4 alkoxycarbonyl, or C1-4 alkylcarbamoyl, or R2 and R3, together with X and Y, form a fused (un)substituted succinimide ring; and R4 and R5 are independently selected from halo, OH, CF3, nitro, amino, cyano, C1-4 alkyl, C1-4 alkoxy, phenoxy, Ph, and (un)substituted sulfamoyl; including salts, stereoisomers, rotamers, tautomers, and racemates thereof. In compds. II, the dotted bond is a single bond or double bond; Z is O or (un)substituted N; R6 is C1-4 alkyl; R7 is absent, H, or OH; R8 and R9 are H or form a single bond together; and R10, R11, and R12 are independently selected from H and OH; including salts, stereoisomers, rotamers, tautomers, and racemates thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I together with a pharmaceutically acceptable adjuvant, as well as to the use of the compns. for the treatment of pain, inflammatory disorders, neurol. disorders, or diseases associated with the genitourinary or gastrointestinal systems. Addition of Grignard reagent from α-bromostyrene to N-methyl-4-piperidinone followed by elimination and Diels-Alder reaction with Et acrylate resulted in the formation of octahydroisoquinoline III, which underwent ester hydrolysis and amidation with 3-aminopyridine to give fused piperidine IV. The compds. of the invention are modulators of gated ion channels, e.g., compound IV expressed an IC50 value above 50 μM in an assay for antagonism of acid-sensing ion channels 1a (ASIC1a).

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1177464 CAPLUS
DOCUMENT NUMBER: 147:469227
TITLE: Indole derivatives as modulators of gated ion channels, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Vohra, Rahul; Wei, Chang-Qing; Gan, Zhonghong; Demnitz, Joachim; Ahring, Philip K.
PATENT ASSIGNEE(S): Painceptor Pharma Corporation, Can.
SOURCE: PCT Int. Appl., 187pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2007115408	A1	20071018	WO 2007-CA594		20070410
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
US 20080004282	A1	20080103	US 2007-786415		20070410
US 20080004306	A1	20080103	US 2007-786419		20070410
US 20080004272	A1	20080103	US 2007-786439		20070410
PRIORITY APPLN. INFO.:			US 2006-791085P	P	20060410
			US 2006-791126P	P	20060410
			US 2006-791175P	P	20060410
			US 2006-791123P	P	20060411

OTHER SOURCE(S): MARPAT 147:469227
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to indole derivs. of formula I, which are modulators of gated ion channels. In compds. I, X and Y together form (un)substituted 5- to 7-membered ring fused with the benzo ring; Z is methylcyclopentyl, CH2, O, NR3, or NOR3, where R3 is H, NH2, C1-4 alkylamino, C1-4 alkyl, C2-5 acyl, C1-4 alkylsulfonyl, (un)substituted benzyl, etc.; R1 is selected from H, C1-4 alkyl, Ph, phenyl-C1-4 alkyl, C1-4 alkoxy-C1-4 alkyl, C1-4 alkylsulfonyl, etc.; and R2 is selected from (un)substituted Ph, (un)substituted naphthyl, (un)substituted pyridinyl, and (un)substituted thienyl; including salts, stereoisomers, rotamers, tautomers, and racemates thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I together with a pharmaceutically acceptable adjuvant, as well as to the use of the compns. for the treatment of pain, inflammatory disorders, neurol. disorders, or diseases associated with the genitourinary or gastrointestinal systems. Bromination of isoquinoline followed by nitration,

N-methylation, and hydride reduction resulted in the formation of tetrahydroisoquinoline II, which underwent hydrogenation, condensation with chloral hydrate and hydroxylamine, and intramol. heterocyclization to yield isatin derivative III. Isatin III was condensed with hydroxylamine, coupled with phenylboronic acid, and cleaved at 160° in a microwave reactor to give nitrile IV. The compds. of the invention are modulators of gated ion channels, e.g., compound IV expressed an IC50 value below 10 μM in an assay for antagonism of acid-sensing ion channels 1a (ASIC1a).

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1176220 CAPLUS
DOCUMENT NUMBER: 147:448653
TITLE: Tetrahydroisoquinoline derivatives as modulators of gated ion channels, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Vohra, Rahul; Gan, Zhonghong; Wei, Chang-Qing; Price, Stephen; Dyke, Hazel Joan; Dechaux, Elsa Amandine
PATENT ASSIGNEE(S): Painceptor Pharma Corporation, Can.
SOURCE: PCT Int. Appl., 151pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2007115410	A1	20071018	WO 2007-CA596		20070410
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080004282	A1	20080103	US 2007-786415		20070410
US 20080004306	A1	20080103	US 2007-786419		20070410
US 20080004272	A1	20080103	US 2007-786439		20070410
PRIORITY APPLN. INFO.:			US 2006-791085P	P	20060410
			US 2006-791126P	P	20060410
			US 2006-791175P	P	20060410
			US 2006-791123P	P	20060411

OTHER SOURCE(S): MARPAT 147:448653
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to tetrahydroisoquinoline derivs. of formula I, which are modulators of gated ion channels. In compds. I, XY is (un)substituted -(CH2)4- or (un)substituted -CH2NHCH2CH2-; Z is C or S; R1 is selected from H, halo, amino, cyano, hydroxy, (un)substituted C1-4 alkyl, (un)substituted C1-4 alkoxy, aryl, 5- to 7-membered heteroaryl,

etc.; R2 is S, O, NH, N(OH), or N(O-C1-4 alkyl); R3 is H, OH, (un)substituted amino, (un)substituted C1-4 alkyl, (un)substituted C1-4 alkoxy, aryl, or 5- to 7-membered heteroaryl; m is 0 or 1; L1 is a bond, O, (CH2)1-4, N(Ac), N(SO2-C1-4 alkyl), or NH, where (CH2)1-4 may be interrupted by NH; L2 is a bond, O, CH2, or NH; and Ar is (un)substituted aryl, (un)substituted 5- to 7-membered heteroaryl, or (un)substituted C5-7 cycloalkyl; including salts, stereoisomers, rotamers, tautomers, and racemates thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I together with a pharmaceutically acceptable adjuvant, as well as to the use of the compns. for the treatment of pain, inflammatory disorders, neurol. disorders, or diseases associated with the genitourinary or gastrointestinal systems. Bromination of isoquinoline followed by nitration, N-ethylation, and hydride reduction resulted in the formation of tetrahydroisoquinoline II, which underwent hydrogenation, condensation with chloral hydrate and hydroxylamine, heterocyclization, and condensation with hydroxylamine to yield tetrahydroisoquinoline derivative III. Tetrahydroisoquinoline III was coupled with phenylboronic acid and cleaved at 160 °C in a microwave reactor to give nitrile IV. The compds. of the invention are modulators of gated ion channels, e.g., compound IV expressed IC50 value below 50 μM in an assay for antagonism of acid-sensing ion channels in Xenopus laevis oocytes.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1176219 CAPLUS

DOCUMENT NUMBER: 147:448637

TITLE: Indole derivatives as modulators of gated ion channels, their preparation, pharmaceutical compositions, and use in therapy

INVENTOR(S): Vohra, Rahul; Gan, Zhonghong; Price, Stephen; Dyke, Hazel Joan

PATENT ASSIGNEE(S): Painceptor Pharma Corporation, Can.

SOURCE: PCT Int. Appl., 111pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2007115409	A1	20071018	WO 2007-CA595		20070410
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080004282	A1	20080103	US 2007-786415		20070410
US 20080004306	A1	20080103	US 2007-786419		20070410
US 20080004272	A1	20080103	US 2007-786439		20070410
PRIORITY APPLN. INFO.:			US 2006-791085P	P	20060410
			US 2006-791126P	P	20060410
			US 2006-791175P	P	20060410

US 2006-791123P P 20060411
OTHER SOURCE(S): MARPAT 147:448637
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to indole derivs. of formula I, which are modulators of gated ion channels. In compds. I, the dotted bonds represent single or double bonds; XY is (un)substituted -(CH2)4- or (un)substituted -CH2NHCH2CH2-; Z is CH2, CH, C(O), N, or NH; R1 is selected from H, (un)substituted C1-4 alkyl, and (un)substituted C1-4 alkoxy; R2 is H, C1-5 alkyl, NH2, C1-4 alkylthio, formyl, C1-4 alkoxyamino, etc.; L is a bond, O, CH2, or NH; and Ar is (un)substituted aryl, (un)substituted 5- to 7-membered heteroaryl, or (un)substituted C5-7 cycloalkyl; including salts, stereoisomers, rotamers, tautomers, and racemates thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I together with a pharmaceutically acceptable adjuvant, as well as to the use of the compns. for the treatment of pain, inflammatory disorders, neurol. disorders, or diseases associated with the genitourinary or gastrointestinal systems. Bromination of isoquinoline followed by nitration, N-ethylation, and hydride reduction resulted in the formation of tetrahydroisoquinoline II, which underwent Suzuki coupling with phenylboronic acid, hydrogenation, and heterocyclization with Et (methylthio)acetate to yield indole derivative III. Indole III was reduced with Raney nickel, condensed with N,N-dimethylformamide di-Me acetal, and condensed with ammonia to give enamine IV. The compds. of the invention are modulators of gated ion channels, e.g., compound IV expressed IC50 value below 50 μM in an assay for antagonism of acid-sensing ion channels in Xenopus laevis oocytes.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1075875 CAPLUS
DOCUMENT NUMBER: 147:444626
TITLE: Transient receptor potential V2 expressed in sensory neurons is activated by probenecid
AUTHOR(S): Bang, Sangsu; Kim, Kyung Yoon; Yoo, Sungjae; Lee, Sang-Heon; Hwang, Sun Wook
CORPORATE SOURCE: Korea University Graduate School of Medicine, Seoul, 136-705, S. Korea
SOURCE: Neuroscience Letters (2007), 425(2), 120-125
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Temperature-activated transient receptor potential ion channels (thermoTRPs) are known to function as ambient temperature sensors and are also involved in peripheral pain sensation. The thermoTRPs are activated by a variety of chems., of which specific activators have been utilized to explore the physiol. of particular channels and sensory nerve subtypes. The use of capsaicin for TRPV1 is an exemplary case for nociceptor studies. In contrast, specific agents for another vanilloid subtype channel, TRPV2 have been lacking. Here, we show that probenecid is able to activate TRPV2 using electrophysiol. and calcium imaging techniques with TRPV2-expressing HEK293T cells. Five other sensory thermoTRPs-TRPV1, TRPV3, TRPV4, TRPM8 and TRPA1-failed to show a response to this drug in the same heterologous expression system, suggesting that

probenecid is a specific activator for TRPV2. Probenecid-evoked responses were also reproduced in a distinct subset of cultured trigeminal neurons that were responsive to 2-aminoethoxydiphenyl borate, a TRPV1-3 activator. The probenecid-sensitive neurons were mainly distributed in a medium to large-diameter population, in agreement with previous observations with TRPV2 immunolocalization. Under inflammation, probenecid elicited nociceptive behaviors in in vivo assays. These results suggest that TRPV2 is specifically activated by probenecid and that this chemical might be useful for investigation of pain-related TRPV2 function.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1029912 CAPLUS

DOCUMENT NUMBER: 147:365488

TITLE: Preparation of heterocyclic compounds as TRPV3 modulators

INVENTOR(S): Chong, Jayhong A.; Fanger, Christopher; Larsen, Glenn R.; Lumma, William C.; Moran, Magdalene M.; Ripka, Amy; Underwood, Dennis John; Weigele, Manfred; Zhen, Xiaoguang

PATENT ASSIGNEE(S): Hydra Biosciences, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 115pp., Cont.-in-part of U.S. Ser. No. 431,942.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070213321	A1	20070913	US 2006-600514	20061115
US 20060270688	A1	20061130	US 2006-431942	20060509
WO 2008060626	A2	20080522	WO 2007-US24100	20071115
WO 2008060626	A9	20080731		

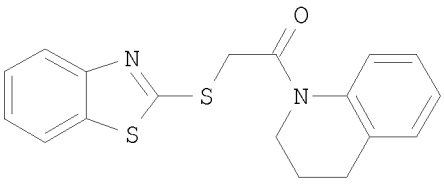
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.:	US 2005-679436P	P	20050509
	US 2005-679438P	P	20050509
	US 2005-702584P	P	20050725
	US 2006-431942	A2	20060509
	US 2006-600514	A1	20061115

OTHER SOURCE(S): MARPAT 147:365488

GI



I

AB The title compds. with general formula of Ar-(X)n-CH(R)-C(=W)-Y [wherein Ar = (hetero)aryl; Y = Ph, OAr1, SAr1, or N(R1)Ar1; R = H or alkyl; X = CH2, O, S, CF2, C(CN)2, or (un)substituted NH; W = O, S, or NR2; n = 1 or 2; Ar1 = monocyclic or bicyclic (hetero)aralkyl or (hetero)aryl; R1 = H, (cyclo)alkyl, alkenyl, alkynyl, heterocyclyl, etc.; R2 = H or alkyl; or R1, N, and R2 form a ring; or R1, Ar1, and N form form a ring fused to Ar1], or solvates, hydrates, metabolites, prodrugs, or salts thereof were prepared as modulators of transient receptor potential cation channel subfamily V member 3 (TRPV3). For example, (2-benzothiazolylthio)acetic acid was reacted with 1,2,3,4-tetrahydroquinoline to give I (82%). I diminished pain phases associated with the formalin model.

L9 ANSWER 13 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:966625 CAPLUS
DOCUMENT NUMBER: 147:292253
TITLE: Methods and compositions for treating hyperalgesia
INVENTOR(S): Patapoutian, Ardem; Jegla, Timothy J.
PATENT ASSIGNEE(S): IRM LLC, A Delaware Limited Liability Company, Bermuda; The Scripps Research Institute
SOURCE: PCT Int. Appl., 33pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2007098252	A2	20070830	WO 2007-US4640		20070221
WO 2007098252	A3	20071018			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2007217512	A1	20070830	AU 2007-217512		20070221
IN 2008DN07492	A	20080926	IN 2008-DN7492		20080903
PRIORITY APPLN. INFO.:			US 2006-775519P	P	20060221
			WO 2007-US4640	W	20070221

AB This invention provides compds. which specifically inhibit TRPA1 but not other members of the thermoTRP ion channel family. Also provided in the invention are methods of using TRPA1-specific inhibitors to treat or alleviate pains mediated by noxious mechanosensation. The physiol. role of TRPA1 in mech. hyperalgesia was demonstrated in CHO cells

transfected with bradykinin B2 receptor and TRPA1. Following pretreatment with bradykinin these cells demonstrated a sensitized TRPA1 sensitized response.

L9 ANSWER 14 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:857076 CAPLUS
DOCUMENT NUMBER: 147:382453
TITLE: TRP channels: Targets for the relief of pain
AUTHOR(S): Levine, Jon D.; Alessandri-Haber, Nicole
CORPORATE SOURCE: Departments of Oral and Maxillofacial Surgery and Medicine and Division of Neurosciences, University of California, San Francisco, CA, 94143-0440, USA
SOURCE: Biochimica et Biophysica Acta, Molecular Basis of Disease (2007), 1772(8), 989-1003
CODEN: BBADEX; ISSN: 0925-4439
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Patients with inflammatory or neuropathic pain experience hypersensitivity to mech., thermal and/or chemical stimuli. Given the diverse etiologies and mol. mechanisms of these pain syndromes, an approach to developing successful therapies may be to target ion channels that contribute to the detection of thermal, mech. and chemical stimuli and promote the sensitization and activation of nociceptors. Transient Receptor Potential (TRP) channels have emerged as a family of evolutionarily conserved ligand-gated ion channels that contribute to the detection of phys. stimuli. Six TRPs (TRPV1, TRPV2, TRPV3, TRPV4, TRPM8 and TRPA1) have been shown to be expressed in primary afferent nociceptors, pain sensing neurons, where they act as transducers for thermal, chemical and mech. stimuli. This short review focuses on their contribution to pain hypersensitivity associated with peripheral inflammatory and neuropathic pain states.
REFERENCE COUNT: 194 THERE ARE 194 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:822522 CAPLUS
DOCUMENT NUMBER: 147:298032
TITLE: Differential expression of the capsaicin receptor TRPV1 and related novel receptors TRPV3, TRPV4 and TRPM8 in normal human tissues and changes in traumatic and diabetic neuropathy
AUTHOR(S): Facer, Paul; Casula, Maria A.; Smith, Graham D.; Benham, Christopher D.; Chessell, Iain P.; Bountra, Chas; Sinisi, Marco; Birch, Rolfe; Anand, Praveen
CORPORATE SOURCE: Peripheral Neuropathy Unit, Imperial College, Hammersmith Hospital, London, UK
SOURCE: BMC Neurology (2007), 7, No pp. given
CODEN: BNMEC8; ISSN: 1471-2377
URL: http://www.biomedcentral.com/content/pdf/1471-2377-7-11.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Transient receptor potential (TRP) receptors expressed by primary sensory neurons mediate thermosensitivity, and may play a role in sensory pathophysiol. We previously reported that human dorsal root ganglion (DRG) sensory neurons co-expressed TRPV1 and TRPV3, and that these were increased in injured human DRG. Related receptors TRPV4, activated by warmth and eicosanoids, and TRPM8, activated by cool and menthol, have been characterised in pre-clin. models. However, the role

of TRPs in common clin. sensory neuropathies needs to be established. We have studied TRPV1, TRPV3, TRPV4, and TRPM8 in nerves (n = 14) and skin from patients with nerve injury, avulsed dorsal root ganglia (DRG) (n = 11), injured spinal nerve roots (n = 9), diabetic neuropathy skin (n = 8), non-diabetic neuropathic nerve biopsies (n = 6), their resp. control tissues, and human post mortem spinal cord, using immunohistol. methods. TRPV1 and TRPV3 were significantly increased in injured brachial plexus nerves, and TRPV1 in hypersensitive skin after nerve repair, while TRPV4 was unchanged. TRPM8 was detected in a few medium diameter DRG neurons, and was unchanged in DRG after avulsion injury, but was reduced in axons and myelin in injured nerves. In diabetic neuropathy skin, TRPV1 expressing sub- and intra-epidermal fibers were decreased, as was expression in surviving fibers. TRPV1 was also decreased in non-diabetic neuropathic nerves. Immunoreactivity for TRPV3 was detected in basal keratinocytes, with a significant decrease of TRPV3 in diabetic skin. TRPV1-immunoreactive nerves were present in injured dorsal spinal roots and dorsal horn of control spinal cord, but not in ventral roots, while TRPV3 and TRPV4 were detected in spinal cord motor neurons. The accumulation of TRPV1 and TRPV3 in peripheral nerves after injury, in spared axons, matches our previously reported changes in avulsed DRG. Reduction of TRPV1 levels in nerve fibers in diabetic neuropathy skin may result from the known decrease of nerve growth factor (NGF) levels. The role of TRPs in keratinocytes is unknown, but a relationship to changes in NGF levels, which is produced by keratinocytes, deserves investigation. TRPV1 represents a more selective therapeutic target than other TRPs for pain and hypersensitivity, particularly in post-traumatic neuropathy.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:703686 CAPLUS
DOCUMENT NUMBER: 147:118255
TITLE: Quinoline and quinazoline compositions and methods for modulating gated ion channels and their preparation
INVENTOR(S): Vohra, Rahul; Babinski, Kazimierz; Brochu, Jean-Louis; Ntirampebura, Deogratias; Wei, Chang-Qing; Zamboni, Robert Joseph
PATENT ASSIGNEE(S): Painceptor Pharma Corporation, Can.
SOURCE: PCT Int. Appl., 155pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007071055	A1	20070628	WO 2006-CA2105	20061221

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2006329202	A1	20070628	AU 2006-329202		20061221
CA 2634491	A1	20070628	CA 2006-2634491		20061221
US 20070197509	A1	20070823	US 2006-643640		20061221
EP 1968968	A1	20080917	EP 2006-840532		20061221
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS					
MX 200807889	A	20080731	MX 2008-7889		20080618
KR 2008089416	A	20081006	KR 2008-717629		20080718
IN 2008DN06306	A	20081024	IN 2008-DN6306		20080718
PRIORITY APPLN. INFO.:			US 2005-753201P	P	20051221
			WO 2006-CA2105	W	20061221

OTHER SOURCE(S): MARPAT 147:118255

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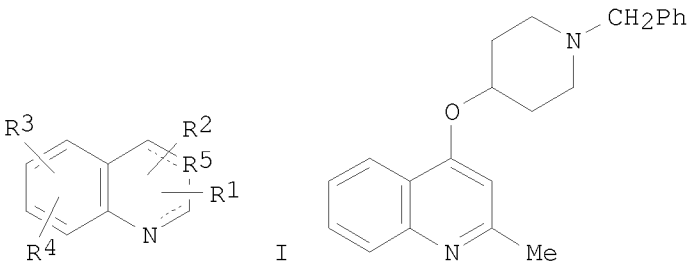

AB Disclosed are quinoline and quinazoline compds. of formula I, which modulate the activity of the gated ion channels compds. that modulate these gated ion channels are useful in the treatment of diseases and disorders related to pam, inflammation, the neurol. system, the gastrointestinal system and genitourinary system. The preferred compds. include quinoline or quinazoline derivs. substituted at the 4- position via N(H), C(O) or O moieties. Compds. of formula I wherein dashed line is single or double bond, wherein when the dashed lines is single bond, N of the ring may be bond to H and R1; R1, R3 and R4 are independently H, (un)substituted amine, CN, NO2, CO2H, and, halo, etc.; R2 is H, (un)substituted amino, amide, halo, NO2, (un)substituted aryl, etc.; R5 is N, C and CH; and their pharmaceutically acceptable salts, enantiomers, stereoisomers, rotamers, tautomers, diastereoisomers, and racemates thereof, are claimed. Example compound II was prepared by substitution of 4-chloro-2-methylquinoline with 1-benzylpiperidin-4-ol. All the invention compds. were evaluated for their gated ion channel modulatory activity.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:671798 CAPLUS
DOCUMENT NUMBER: 147:51037
TITLE: Genetic polymorphisms associated with an increased risk of somatosensory disorders and their use in diagnosis, prognosis, and selection of therapies
INVENTOR(S): Diatchenko, Luda; Maixner, William
PATENT ASSIGNEE(S): The University of North Carolina at Chapel Hill, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007070252	A2	20070621	WO 2006-US45757	20061129
WO 2007070252	A3	20071221		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

CA 2631675	A1	20070621	CA 2006-2631675	20061129
EP 1951910	A2	20080806	EP 2006-848638	20061129

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS

PRIORITY APPLN. INFO.:	US 2005-740937P	P	20051130
	US 2006-815982P	P	20060623
	WO 2006-US45757	W	20061129

AB Methods of predicting effective pharmacol. therapies for a subject afflicted with a somatosensory disorder by determining a genotype of the subject with or without determination of psychosocial and/or neurol. assessments of the subject are provided. Methods of predicting susceptibility of a subject to develop somatosensory disorders by determining a genotype of the subject with or without determination of psychosocial and/or neurol. assessments of the subject are further provided.

L9 ANSWER 18 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2007:616985 CAPLUS
DOCUMENT NUMBER:	147:70137
TITLE:	Increased TRPA1, TRPM8, and TRPV2 expression in dorsal root ganglia by nerve injury
AUTHOR(S):	Frederick, J.; Buck, M. E.; Matson, D. J.; Cortright, D. N.
CORPORATE SOURCE:	Western Connecticut State University, Danbury, CT, 06810, USA
SOURCE:	Biochemical and Biophysical Research Communications (2007), 358(4), 1058-1064 CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER:	Elsevier
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Thermosensitive TRP channels display unique thermal responses, suggesting distinct roles mediating sensory transmission of temperature However, whether relative expression of these channels in dorsal root ganglia (DRG) is altered in nerve injury is unknown. The authors developed a multiplex RNase protection assay (RPA) to quantify rat TRPV1, TRPV2, TRPV3, TRPV4, TRPA1, and TRPM8 RNA levels in DRG. The authors used the multiplex RPA to measure thermosensitive TRP channel RNA levels in DRG from RTX-treated rats (300 μg/kg) or rats with unilateral sciatic nerve chronic constriction injury (CCI). TRPV1 and TRPA1 RNA were significantly decreased in DRG from RTX-treated rats, indicating functional colocalization of TRPA1 and TRPV1 in sensory nociceptors. In DRG from CCI rats, TRPA1, TRPV2, and TRPM8 RNA showed slight but significant increases

ipsilateral to peripheral nerve injury. The authors' findings support the hypothesis that increased TRP channel expression in sensory neurons may contribute to mech. and cold hypersensitivity.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:590735 CAPLUS
DOCUMENT NUMBER: 147:30964
TITLE: Pyrroloisoquinolines and their preparation, compositions and methods for modulating gated ion channels
INVENTOR(S): Vohra, Rahul; Demnitz, Joachim; Ahring, Philip K.; Gan, Zhonghong; Gill, Nachhattarpal
PATENT ASSIGNEE(S): Painceptor Pharma Corporation, Can.
SOURCE: PCT Int. Appl., 118pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2007059608	A1	20070531	WO 2006-CA1897		20061122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006317545	A1	20070531	AU 2006-317545		20061122
CA 2630617	A1	20070531	CA 2006-2630617		20061122
US 20070191418	A1	20070816	US 2006-603946		20061122
EP 1957486	A1	20080820	EP 2006-804755		20061122
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS					
KR 2008070749	A	20080730	KR 2008-714653		20080617
IN 2008DN05376	A	20080808	IN 2008-DN5376		20080620
PRIORITY APPLN. INFO.:			US 2005-739600P	P	20051123
			WO 2006-CA1897	W	20061122

OTHER SOURCE(S): MARPAT 147:30964
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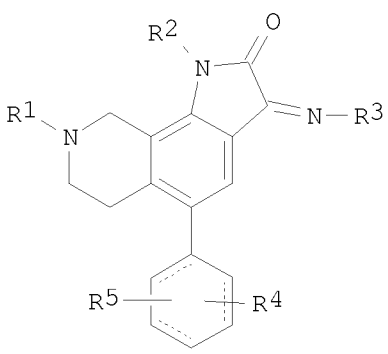

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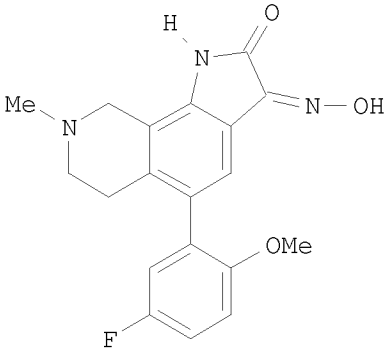

II

AB Pyrrolo-isoquinoline compds. according to formula I is disclosed. Compds. of formula I wherein dashed lines are single or double bonds; R1 is H, alkyl, alkoxy-alkyl, hydroxyalkyl, alkoxycarbonyl-alkyl, etc.; R2 is H, OH, alkyl, alkenyl, (CH2)1-4CO2H, CO-C1-4 alkyl, and SO2-C1-4 alkyl; R3 is H, OH, alkyl, acyl, benzyl, CO2H, CONMe2, OPh, OCF3, alkoxy, etc.; R4 and R5 are independently halo, CF3, NO2, NH2, CN, OH, alkoxy, PhO, Ph, SO2NH2 and derivs.; and their pharmaceutically acceptable salts, enantiomers, stereoisomers, rotamers, tautomers, diastereoisomers, and racemates thereof, are claimed. These compds. and their pharmaceutical acceptable salts are used for modulating gated ion channels in order to treat pain, inflammatory disorders, neurol. disorders, or diseases associated with the genitourinary or gastrointestinal systems. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their ASIC antagonistic activity. From the assay, it was determined that compound II exhibited IC50 values of 0.10-0.20 μM.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:538923 CAPLUS
DOCUMENT NUMBER: 146:521819
TITLE: Dihydroquinazolinone compounds for modulating TRPV3 function and their preparation, pharmaceutical compositions and use in the treatment of pain and related disorders
INVENTOR(S): Chong, Jayhong A.; Fanger, Christopher; Larsen, Glenn R.; Lumma, William C., Jr.; Moran, Magdalene M.; Ripka, Amy; Underwood, Dennis John; Weigele, Manfred; Zhen, Xiaoguang
PATENT ASSIGNEE(S): Hydra Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 202pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007056124	A2	20070518	WO 2006-US42930	20061103
WO 2007056124	A3	20070726		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,

KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

AU 2006311883	A1	20070518	AU 2006-311883	20061103
CA 2628441	A1	20070518	CA 2006-2628441	20061103
US 20070179164	A1	20070802	US 2006-592783	20061103
EP 1954283	A2	20080813	EP 2006-836869	20061103
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.:

US 2005-733384P	P	20051104
US 2006-799212P	P	20060509
US 2006-838609P	P	20060818
WO 2006-US42930	W	20061103

OTHER SOURCE(S): MARPAT 146:521819

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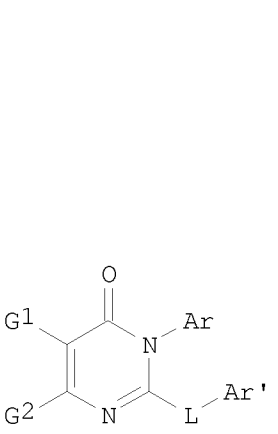

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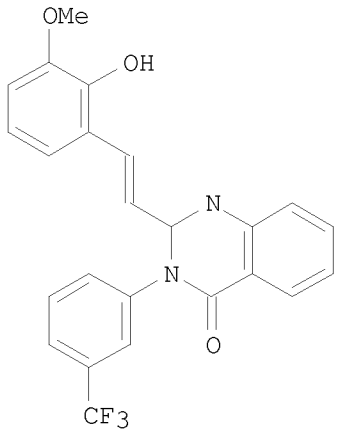

II

AB The application relates to compds. of formula I and methods for treating pain and other conditions related to TRPV3. Compds. of formula I wherein Ar and Ar' are independently (hetero)aryl; G1 and G2 are independently lower alkyl; G1G2 taken together to form (hetero)aryl fused to the pyrimidinone ring; L is a linker having 1-3 atoms; and their salts, solvates, hydrated, oxidative metabolites and prodrugs thereof, are claimed. Example compound II was prepared by condensation of 2-methyl-4H-3,1-benzoxazin-4-one with 3-trifluoromethylaniline; the resulting 2-methyl-3-(3-trifluoromethylphenyl)quinazolin-4(3H)-one underwent condensation with 2-hydroxy-3-methoxybenzaldehyde. All the invention compds. were evaluated for their TRPV3 modulatory activity.

L9 ANSWER 21 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2007:335876 CAPLUS
DOCUMENT NUMBER:	147:273373
TITLE:	Nociception and TRP channels
AUTHOR(S):	Tominaga, M.
CORPORATE SOURCE:	Section of Cell Signaling, Okazaki Institute for Integrative Bioscience, National Institutes of Natural Sciences, Okazaki, 444-8787, Japan

SOURCE: Handbook of Experimental Pharmacology (2007), 179(Transient Receptor Potential (TRP) Channels), 489-505
CODEN: HEPHD2; ISSN: 0171-2004
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Pain is initiated when noxious stimuli excite the peripheral terminals of specialized primary afferent neurons called nociceptors. Many mols. are involved in conversion of the noxious stimuli to the elec. signals in the nociceptor endings. Among them, TRP channels play important roles in detecting noxious stimuli.
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 22 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:177123 CAPLUS
DOCUMENT NUMBER: 146:202886
TITLE: The identification of two novel ion channels, TRPV3 and TRPV4 and the elucidation of their roles in temperature and pain sensation
AUTHOR(S): Lee, Hyosang
CORPORATE SOURCE: Johns Hopkins Univ., Baltimore, MD, USA
SOURCE: (2006) 147 pp. Avail.: UMI, Order No. DA3213744
From: Diss. Abstr. Int., B 2006, 67(4), 1851
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L9 ANSWER 23 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1202500 CAPLUS
DOCUMENT NUMBER: 145:505435
TITLE: Benzothiazole derivatives and related compounds for modulating TRPV3 function and their preparation, pharmaceutical compositions and their use for treatment of pain
INVENTOR(S): Chong, Jayhong A.; Fanger, Christopher; Moran, Magdalena M.; Underwood, Dennis John; Zhen, Xiaoguang; Ripka, Amy; Weigele, Manfred; Lumma, William C., Jr.; Larsen, Glenn R.
PATENT ASSIGNEE(S): Hydra Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 237pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006122156	A2	20061116	WO 2006-US17995	20060509
WO 2006122156	A3	20070201		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2006244074	A1	20061116	AU 2006-244074		20060509
CA 2608194	A1	20061116	CA 2006-2608194		20060509
EP 1888575	A2	20080220	EP 2006-759445		20060509
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CN 101233132	A	20080730	CN 2006-80025106		20080109
PRIORITY APPLN. INFO.:			US 2005-679436P	P	20050509
			US 2005-679438P	P	20050509
			US 2005-702584P	P	20050725
			WO 2006-US17995	W	20060509

OTHER SOURCE(S): MARPAT 145:505435

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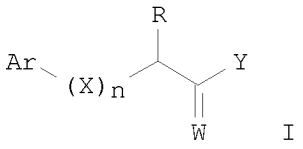

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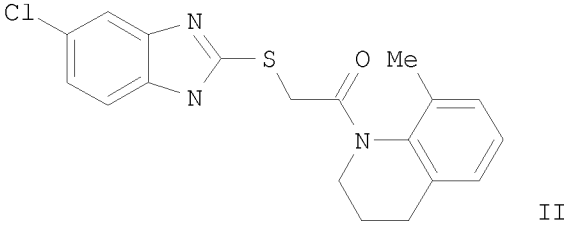


II

AB The application relates to compds. of formula I and methods for treating pain and other conditions related to TRPV3. Compds. of formula I wherein Ar is (hetero)aryl; Y is Ph, (hetero)arylalkyloxy, (hetero)aryloxy, (hetero)arylalkylthio, (hetero)arylthio, (hetero)arylalkylamino, (hetero)arylamino, etc.; R is H and lower alkyl; X is CH2, O, S, NH and derivs., CF2, C(CN)2; W is O, S and NH and derivs.; n is 1; when X is CH2 n is 1 and 2; and their pharmaceutically acceptable salts, solvates, oxidative metabolites, and prodrugs thereof are claimed. Example compound II was prepared by thioetherification of N-(chloroacetyl)-8-methyl-1,2,3,4-tetrahydroquinoline with 5-chloro-2-mercaptobenzothiazole. All the invention compds. were evaluated for their TRPV3 inhibitory activity. Several of the tested compds. exhibited IC50 values of 1000 nM or less. Example compound II exhibited an IC50 value of < 0.2 μM.

L9 ANSWER 24 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2006:811801 CAPLUS
DOCUMENT NUMBER:	145:284902
TITLE:	More than cool: Promiscuous relationships of menthol and other sensory compounds
AUTHOR(S):	Macpherson, Lindsey J.; Hwang, Sun Wook; Miyamoto, Takashi; Dubin, Adrienne E.; Patapoutian, Ardem; Story, Gina M.
CORPORATE SOURCE:	Department of Cell Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE:	Molecular and Cellular Neuroscience (2006), 32(4),

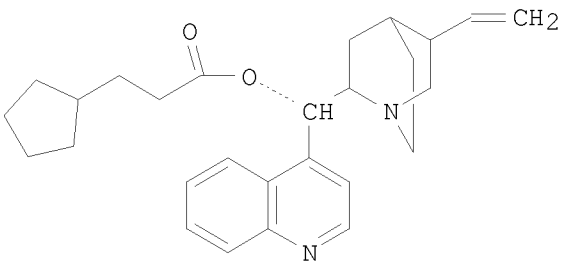
335-343
CODEN: MOCNED; ISSN: 1044-7431
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several temperature-activated transient receptor potential (thermoTRP) ion channels are the mol. receptors of natural compds. that evoke thermal and pain sensations. Menthol, popularly known for its cooling effect, activates TRPM8 - a cold-activated thermoTRP ion channel. However, human physiol. studies demonstrate a paradoxical role of menthol in modulation of warm sensation, and here, we show that menthol also activates heat-activated TRPV3. We further show that menthol inhibits TRPA1, potentially explaining the use of menthol as an analgesic. Similar to menthol, both camphor and cinnamaldehyde (initially reported to be specific activators of TRPV3 and TRPA1, resp.) also modulate other thermoTRPs. Therefore, we find that many "sensory compds." presumed to be specific have a promiscuous relationship with thermoTRPs.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 25 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:343936 CAPLUS
DOCUMENT NUMBER: 144:382035
TITLE: Compositions and therapeutic methods using cyclic and heterocyclic compound gated ion channel modulators
INVENTOR(S): Babinski, Kazimierz; Szarek, Walter A.; Vohra, Rahul; Varming, Thomas; Ahring, Philip K.; Dyhring Joergensen, Tino; Blackburn-Munro, Gordon John
PATENT ASSIGNEE(S): Painceptor Pharma Corp., Can.; Neurosearch A/S
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006038070	A2	20060413	WO 2005-IB2613	20050330
WO 2006038070	A3	20060601		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2561993	A1	20060413	CA 2005-2561993	20050330
EP 1734962	A2	20061227	EP 2005-805035	20050330
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
US 20070004680	A1	20070104	US 2005-96239	20050330
JP 2007530664	T	20071101	JP 2007-505676	20050330
PRIORITY APPLN. INFO.:			US 2004-558059P P	20040330
			US 2004-564063P P	20040420
			WO 2005-IB2613 W	20050330

OTHER SOURCE(S): MARPAT 144:382035

GI



I

AB The invention discloses compns. and therapeutic methods using cyclic and heterocyclic compound gated ion channel modulators. Tested compds. include e.g. I.

L9 ANSWER 26 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1324927 CAPLUS
DOCUMENT NUMBER: 144:101461
TITLE: NGF rapidly increases membrane expression of TRPV1 heat-gated ion channels
AUTHOR(S): Zhang, Xuming; Huang, Jiehong; McNaughton, Peter A.
CORPORATE SOURCE: Department of Pharmacology, University of Cambridge, Cambridge, UK
SOURCE: EMBO Journal (2005), 24(24), 4211-4223
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nociceptors, or pain-sensitive receptors, are unique among sensory receptors in that their sensitivity is increased by noxious stimulation. This process, called sensitization or hyperalgesia, is mediated by a variety of proinflammatory factors, including bradykinin, ATP and NGF, which cause sensitization to noxious heat stimuli by enhancing the membrane current carried by the heat- and capsaicin-gated ion channel, TRPV1. Several different mechanisms for sensitization of TRPV1 have been proposed. Here we show that NGF, acting on the TrkA receptor, activates a signaling pathway in which PI3 kinase plays a crucial early role, with Src kinase as the downstream element which binds to and phosphorylates TRPV1. Phosphorylation of TRPV1 at a single tyrosine residue, Y200, followed by insertion of TRPV1 channels into the surface membrane, explains most of the rapid sensitizing actions of NGF.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 27 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:298408 CAPLUS
DOCUMENT NUMBER: 142:314533
TITLE: Increased capsaicin receptor TRPV1 in skin nerve fibres and related vanilloid receptors TRPV3 and TRPV4 in keratinocytes in human breast pain
AUTHOR(S): Gopinath, Preethi; Wan, Elaine; Holdcroft, Anita; Facer, Paul; Davis, John B.; Smith, Graham D.; Bountra, Chas; Anand, Praveen
CORPORATE SOURCE: Peripheral Neuropathy Unit, Hammersmith Hospital, Faculty of Medicine, Imperial College London, London, UK
SOURCE: BMC Women's Health (2005), 5, No pp. given

CODEN: BWHMAY; ISSN: 1472-6874
URL: http://www.biomedcentral.com/content/pdf/1472-6874-5-2.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Breast pain and tenderness affects 70% of women at some time. These symptoms have been attributed to stretching of the nerves with increase in breast size, but tissue mechanisms are poorly understood. Methods: Eighteen patients (n = 12 breast reduction and n = 6 breast reconstruction) were recruited and assessed for breast pain by clin. questionnaire. Breast skin biopsies from each patient were examined using immunohistol. methods with specific antibodies to the capsaicin receptor TRPV1, related vanilloid thermoreceptors TRPV3 and TRPV4, and nerve growth factor (NGF). Results: TRPV1-pos. intra-epidermal nerve fibers were significantly increased in patients with breast pain and tenderness (TRPV1 fibers / mm epidermis, median [range] - no pain group, n=8, 0.69 [0-1.27]; pain group, n=10, 2.15 [0.77 - 4.38]; p=0.0009). Nerve Growth Factor, which up-regulates TRPV1 and induces nerve sprouting, was present basal keratinocytes: some breast pain specimens also showed NGF staining in supra-basal keratinocytes. TRPV4-immunoreactive fibers were present in sub-epidermis but not significantly changed in painful breast tissue. Both TRPV3 and TRPV4 were significantly increased in keratinocytes in breast pain tissues; (TRPV3, median [range] - no pain group, n=6, 0.75 [0-2]; pain group, n = 11, 2 [1 - 3], p=0.008; TRPV4, median [range] - no pain group, n = 6, [0-1]; pain group, n=11, 1 [0.5 - 2], p=0.014). Conclusions: Increased TRPV1 intra-epidermal nerve fibers could represent collateral sprouts, or re-innervation following nerve stretch and damage by polymodal nociceptors. Selective TRPV1-blockers may provide new therapy in breast pain. The role of TRPV3 and TRPV4 changes in keratinocytes deserve further study.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 28 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:176855 CAPLUS
DOCUMENT NUMBER: 142:237148
TITLE: Impaired Thermosensation in Mice Lacking TRPV3, a Heat and Camphor Sensor in the Skin
AUTHOR(S): Moqrich, Aziz; Hwang, Sun Wook; Earley, Taryn J.; Petrus, Matt J.; Murray, Amber N.; Spencer, Kathryn S. R.; Andahazy, Mary; Story, Gina M.; Patapoutian, Ardem
CORPORATE SOURCE: Department of Cell Biology, Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Science (Washington, DC, United States) (2005), 307(5714), 1468-1472
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Environmental temperature is thought to be directly sensed by neurons through their projections in the skin. A subset of the mammalian transient receptor potential (TRP) family of ion channels has been implicated in this process. These "thermoTRPs" are activated at distinct temperature thresholds and are typically expressed in sensory neurons. TRPV3 is activated by heat (>33°) and, unlike most thermoTRPs, is expressed in mouse keratinocytes. We found that TRPV3 null mice have strong deficits in responses to innocuous and noxious heat but not in other sensory modalities; hence, TRPV3 has a specific role in thermosensation. The natural compound camphor, which modulates sensations

of warmth in humans, proved to be a specific activator of TRPV3. Camphor activated cultured primary keratinocytes but not sensory neurons, and this activity was abolished in TRPV3 null mice. Therefore, heat-activated receptors in keratinocytes are important for mammalian thermosensation.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 29 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:64723 CAPLUS
DOCUMENT NUMBER: 142:237058
TITLE: The Temperature-Sensitive Ion Channel TRPV2 is Endogenously Expressed and Functional in the Primary Sensory Cell Line F-11
AUTHOR(S): Bender, Florian; Mederos y Schnitzler, Michael; Li, Yanzhang; Ji, Ailing; Weihe, Eberhard; Gudermann, Thomas; Schaefer, Martin
CORPORATE SOURCE: Molecular Neuroscience, Institute of Anatomy and Cell Biology, Philipps University Marburg, Marburg, Germany
SOURCE: Cellular Physiology and Biochemistry (2005), 15(1-4), 183-194
CODEN: CEPBEW; ISSN: 1015-8987
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In sensory neurons heat is transduced by a subfamily of TRP channels sharing sequence homol. with the capsaicin-sensitive vanilloid receptor subtype 1 (TRPV1), but differing in their thermal response thresholds. To identify a neuronal cell line endogenously expressing noxious heat-transducing ion channels, we examined F-11 cells, a hybridoma derived from rat dorsal root ganglia and mouse neuroblastoma. Using RT-PCR, transcripts homologous to TRPV2 and TRPV4, but not to TRPV1 or TRPV3, were found. We isolated a full-length cDNA of 2.4 kb coding for a 757-amino acid protein corresponding to mouse TRPV2, which was further characterized by immunocytochem. and electrophysiol. Using the whole-cell patch-clamp technique, we observed a heat-evoked increase in outward and inward currents with a threshold of 51.6 ± 0.2°C. The current-voltage relationship stimulated by a temperature of 52°C was characterized by an outward rectification with a reversal potential close to -10 mV. Heat-evoked currents could be inhibited by ruthenium red. There was no activation by stimulation with capsaicin or 2-aminoethoxydiphenyl borate. Our results indicate that F-11 cells express functional noxious heat-sensitive TRPV2 channels. Thus, we propose that F-11 cells represent a valuable in vitro model to characterize the properties of TRPV2 in a native neuronal environment.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 30 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:50668 CAPLUS
DOCUMENT NUMBER: 142:152793
TITLE: The role of TRP channels in sensory neurons
AUTHOR(S): Koltzenburg, Martin
CORPORATE SOURCE: Neural Plasticity Unit, Institute of Child Health, London, WC1N 1EH, UK
SOURCE: Novartis Foundation Symposium (2004), 260(Osteoarthritic Joint Pain), 206-220
CODEN: NFSYF7; ISSN: 1528-2511
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Two parallel processes characterize the contemporary

pain field. Firstly, enormous progress is being made in the discovery of the cellular and mol. mechanisms responsible for the pathogenesis of pain and secondly, there is a growing appreciation that multiple mechanisms contribute to common clin. pain syndromes. The aim of this chapter is to provide a short overview how transient receptor potential (TRP) channels could contribute to acute and chronic pain states. TRP channels of the vanilloid family (TRPV1, TRPV2, TRPV3, TRPV4) are excited by heat stimuli whereas TRPM8 and ANKTM1 are cold responsive. TRPV1 and ANKTM1 are mediating the pungency of nociceptor-specific chems. such as capsaicin or mustard oil. Sensitization of TRPV1 is an important mechanisms for heat hyperalgesia and thus the generation of chronic pain symptoms.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 31 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:15176 CAPLUS
DOCUMENT NUMBER: 142:90823
TITLE: Nociception and TRP channels
AUTHOR(S): Numazaki, Mitsuko; Tominaga, Makoto
CORPORATE SOURCE: Department of Anesthesiology, University of Tsukuba School of Medicine, Tsukuba, 305-0006, Japan
SOURCE: Current Drug Targets: CNS & Neurological Disorders (2004), 3(6), 479-485
CODEN: CDTCCC; ISSN: 1568-007X
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Noxious thermal, mech., or chemical stimuli evoke pain through excitation of the peripheral terminals called nociceptor, and many kinds of ionotropic and metabotropic receptors are involved in this process. Capsaicin receptor TRPV1 is a nociceptor-specific ion channel that serves as the mol. target of capsaicin. TRPV1 can be activated not only by capsaicin but also by noxious heat (with a thermal threshold >43°) or protons (acidification), all of which are known to cause pain in vivo. Studies using TRPV1-deficient mice have shown that TRPV1 is essential for selective modalities of pain sensation and for thermal hyperalgesia. One mechanism underlying inflammatory pain which is initiated by tissue damage/inflammation and characterized by hypersensitivity is sensitization of TRPV1. In addition to TRPV1, there are five thermosensitive ion channels in mammals, all of which belong to the TRP (transient receptor potential) super family. These include TRPV2, TRPV3, TRPV4, TRPM8 and TRPA1. These channels exhibit distinct thermal activation thresholds (> 52° for TRPV2, > .apprx.34-38° for TRPV3, > .apprx.27-35° for TRPV4, < .apprx.25-28° for TRPM8 and < 17° for TRPA1) and are expressed in primary sensory neurons as well as other tissues. Some of the thermosensitive TRP channels are likely to be involved in thermal nociception, since their activation thresholds are within the noxious range of temps.

REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 32 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:836627 CAPLUS
DOCUMENT NUMBER: 141:345114
TITLE: Molecular mechanisms of thermosensation
AUTHOR(S): Tominaga, Makoto
CORPORATE SOURCE: Sect. Cell Signaling, Okazaki Inst. Integr. Biosci., Natl. Inst. Nat. Sci., Okazaki, 444-8787, Japan
SOURCE: Nippon Yakurigaku Zasshi (2004), 124(4), 219-227
CODEN: NYKZAU; ISSN: 0015-5691

PUBLISHER: Nippon Yakuri Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. We feel a wide range of temps. spanning from cold to heat. Within this range, temps. over about 43° and below about 15° evoke not only a thermal sensation, but also a feeling of pain. In mammals, six thermosensitive ion channels have been reported, all of which belong to the TRP (transient receptor potential) super family. These include TRPV1 (VR1), TRPV2 (VRL-1), TRPV3, TRPV4, TRPM8 (CMR1), and TRPA1 (ANKTM1). These channels exhibit distinct thermal activation thresholds (>43° for TRPV1, >52° for TRPV2, >32-39° for TRPV3, >27-35° for TRPV4, <25-28° for TRPM8, and <17° for TRPA1) and are expressed in primary sensory neurons as well as other tissues. The involvement od TRPV1 in thermal nociception has been demonstrated by multiple methods, including the anal. of TRPV1-deficient mice. Temperature thresholds for activation of TRPV1, TRPV4, and TRPM8 are not fixed but changeable. Reduction of the temperature threshold for TRPV1 activation is thought to be one mechanism of inflammatory pain. Significant advances in thermosensation research have been made in the last several years with the cloning and characterization of thermosensitive TRP channels. With these clones in hand, we can begin to understand thermosensation from a mol. standpoint.

L9 ANSWER 33 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:679239 CAPLUS
DOCUMENT NUMBER: 141:236376
TITLE: 2-Aminoethoxydiphenyl Borate Is a Common Activator of TRPV1, TRPV2, and TRPV3
AUTHOR(S): Hu, Hong-Zhen; Gu, Qihai; Wang, Chunbo; Colton, Craig K.; Tang, Jisen; Kinoshita-Kawada, Mariko; Lee, Lu-Yuan; Wood, Jackie D.; Zhu, Michael X.
CORPORATE SOURCE: Department of Physiology and Cell Biology, The Ohio State University, Columbus, OH, 43210, USA
SOURCE: Journal of Biological Chemistry (2004), 279(34), 35741-35748
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The transient receptor potential (TRP) superfamily contains a large number of proteins encoding cation permeable channels that are further divided into TRPC (canonical), TRPM (melastatin), and TRPV (vanilloid) subfamilies. Among the six TRPV members, TRPV1, TRPV2, TRPV3, and TRPV4 form heat-activated cation channels, which serve diverse functions ranging from nociception to osmolality regulation. Although chemical activators for TRPV1 and TRPV4 are well documented, those for TRPV2 and TRPV3 are lacking. Here we show that in the absence of other stimuli, 2-aminoethoxydiphenyl borate (2APB) activates TRPV1, TRPV2, and TRPV3, but not TRPV4, TRPV5, and TRPV6 expressed in HEK293 cells. In contrast, 2APB inhibits the activity of TRPC6 and TRPM8 evoked by 1-oleolyl-2-acetyl-sn-glycerol and menthol, resp. In addition, low levels of 2APB strongly potentiate the effect of capsaicin, protons, and heat on TRPV1 as well as that of heat on TRPV3 expressed in Xenopus oocytes. In dorsal root ganglia neurons, supra-additive stimulations were evoked by 2APB and capsaicin or 2APB and acid. Our data suggest the existence of a common activation mechanism for TRPV1, TRPV2, and TRPV3 that may serve as a therapeutic target for pain management and treatment for diseases caused by hypersensitivity and temperature misregulation.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 34 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:634619 CAPLUS
TITLE: TRPV channels in pain
AUTHOR(S): Caterina, Michael
CORPORATE SOURCE: Department of Biological Chemistry, Johns Hopkins University, School of Medicine, Baltimore, MD, 21205, USA
SOURCE: Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), MEDI-009. American Chemical Society: Washington, D. C.
CODEN: 69EKY9
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB The TRPV ion channel subfamily is of considerable interest in the context of its involvement in nociception and other sensory processes. The founding member, TRPV1 (VR1) is highly expressed in a subset of small-to-medium diameter sensory neurons and is activated by capsaicin and pungent vanilloids, protons, noxious heat (> 42°C) or a variety of lipid compds. Mice lacking TRPV1 are insensitive to vanilloids and defective in the detection of noxious heat (e.g. inflammatory thermal hyperalgesia). TRPV2 (VRL-1) is expressed in a subset of medium-to-large diameter neurons and is activated by very high temps. (> 52°C) or growth factors. TRPV3 and TRPV4 are warmth-gated ion channels with a slightly lower activation threshold (.apprx.33°C). TRPV4 can alternatively be activated by the phorbol derivative, 4a phorbol 12,13-didecanoate or by hypoosmolarity and may participate in mechanosensation.

L9 ANSWER 35 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:463560 CAPLUS
DOCUMENT NUMBER: 139:50112
TITLE: Molecular mechanisms of nociception and thermosensation: structures, expressions and functions of capsaicin receptor and its homologues
AUTHOR(S): Numazaki, Mitsuko; Tominaga, Makoto
CORPORATE SOURCE: Cell. Mol. Phaysiol., Mie Univ. Sch. Med., Tsu, 514-8507, Japan
SOURCE: Seikagaku (2003), 75(5), 359-371
CODEN: SEIKAQ; ISSN: 0037-1017
PUBLISHER: Nippon Seikagakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review on (1) structure and classification of transient receptor potential (TRP) cation channel superfamily, (2) electrophysiol. characteristics, structure-function relationship, reception of multiple pain stimuli (capsaicin, acid, and heat), activation regulation, tissue distribution, agonists, and antagonists of TRPV1 (capsaicin receptor), and (3) TRPV1 homolog involved in thermosensation (TRPV2 for noxious heat, TRPV3 and TRPV4 for warm temps., and TRPM8 for cold temps.).

L9 ANSWER 36 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:964512 CAPLUS
DOCUMENT NUMBER: 138:50915
TITLE: Vanilloid receptor-related nucleic acids and polypeptides and their use for treating pain and screening for therapeutic agents
INVENTOR(S): Patapoutian, Ardem; Song, Chuanzheng; Ganju, Pamposh;

Peier, Andrea; McIntyre, Peter; Bevan, Stuart
PATENT ASSIGNEE(S): Novartis AG, Switz.; Irm LLC
SOURCE: PCT Int. Appl., 197 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002101045	A2	20021219	WO 2002-EP6520	20020613
WO 2002101045	A3	20031120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2450113	A1	20021219	CA 2002-2450113	20020613
AU 2002345844	A1	20021223	AU 2002-345844	20020613
US 20030157633	A1	20030821	US 2002-171319	20020613
US 7115414	B2	20061003		
EP 1399558	A2	20040324	EP 2002-778891	20020613
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005500028	T	20050106	JP 2003-503795	20020613
US 20060251648	A1	20061109	US 2006-384955	20060320
US 7396910	B2	20080708		
US 20080076136	A1	20080327	US 2006-386249	20060321
AU 2006252263	A1	20070125	AU 2006-252263	20061222

PRIORITY APPLN. INFO.:			
US 2001-297835P	P	20010613	
US 2002-351238P	P	20020122	
US 2002-352914P	P	20020129	
US 2002-357161P	P	20020212	
US 2002-381086P	P	20020515	
US 2002-381739P	P	20020516	
US 2002-315238P	P	20020122	
US 2002-171319	A1	20020613	
WO 2002-EP6520	W	20020613	

AB This invention provides novel human genes and polypeptides of the vanilloid receptor (VR) family, identification of trkA pain -specific genes expressed in the dorsal root ganglia, and use of these genes and polypeptides for the treatment of pain and identification of agents useful in the treatment of pain. In particular, cDNA and protein sequences are provided for human and murine TRPV3 (previously known as VRLS, VRLX, VR4, and TRPV7), TRPV4 (previously known as VRL3 and OTRPC4), and TRPM8 (previously known as TRPX). The genes are expressed in either keratinocytes or the dorsal root ganglia, and both TRPV3 and TRPM8 proteins function in temperature sensation. In addition, expression of TRPV3 and TRPV4 genes is up-regulated in a rat injury model.

L9 ANSWER 37 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2008672659 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 18930858
TITLE: Menthol derivative WS-12 selectively activates transient receptor potential melastatin-8 (TRPM8) ion channels.
AUTHOR: Ma Sherkheli; G Gisselmann; Ak Vogt-Eisele; Jf Doerner; H Hatt
CORPORATE SOURCE: Department of Cell Physiology, Faculty of Biology &

Biotechnology, Ruhr-University-Bochum, University Street 150, Bochum 44801, Germany.
SOURCE: Pakistan journal of pharmaceutical sciences, (2008 Oct) Vol. 21, No. 4, pp. 370-8.
Journal code: 9426356. ISSN: 1011-601X.
PUB. COUNTRY: Pakistan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 21 Oct 2008
Last Updated on STN: 21 Oct 2008

AB Transient receptor potential melastatin-8 (TRPM8), a cationic ion channel is involved in detection of normal cooling-sensation in mammals. TRPM8 activation by cooling or chemical agonists have been shown to produce profound, mechanistically novel analgesia in chronic pain states such as neuropathic pain in rodents. Known TRPM8 agonists such as menthol and icilin have a relatively low potency and cross-activate nociceptors like TRPA1; thus bearing a limited therapeutic usefulness. For that reason, characterising ligands, which selectively activate TRPM8, presents a clinical need. Using Xenopus laevis oocytes as expression system, we evaluated WS-12, a menthol derivative, for its potential interaction with all six thermo-sensitive TRP ion channels. Oocytes were injected with cRNA of gene of interest and incubated for 3-5 days (at 16 degrees C) before testing for functional characterisation of the recombinant ion channels. Oocytes were superfused with the test and standard substances respectively. Responses were measured by two-electrode voltage clamp technique and the amplitudes of evoked currents were compared with baseline values. WS-12 robustly activated TRPM8 in low micromolar concentrations (EC50 12+/-5 muM) thereby displaying a higher potency and efficacy compared to menthol (EC50 196+/-22 muM). Any of the other described thermo-sensitive TRP ion channel including TRPV1, TRPV2, TRPV3, TRPV4 and TRPA1 were not activated at a concentration (1 mM) optimally effective for TRPM8 responses; a characteristic which is in sharp contrast to menthol as it activates TRPA1 and TRPV3 in addition to TRPM8. Unlike icilin (75% reduction; $p<0.001$, n=6), WS-12 does not induce tachyphylaxis (4+/-2.3% increase in responses; $p<0.08$, n=6) of TRPM8 mediated currents to repeated exposure of 1 mM doses. In addition, acidosis or variations in extracellular calcium have no influence on potency/efficacy of WS-12 for TRPM8. The selectivity profile of WS-12, its several-fold higher potency and around two-fold increase in efficacy compared to menthol warrants its potential utility for therapy in chronic neuropathic pain states and as a diagnostic probe in prostate cancer.

L9 ANSWER 38 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2008299125 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18461159
TITLE: Citral sensing by TRANSient receptor potential channels in dorsal root ganglion neurons.
AUTHOR: Stotz Stephanie C; Vriens Joris; Martyn Derek; Clardy Jon; Clapham David E
CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Cardiology, Children's Hospital, Boston, Massachusetts, United States of America.
CONTRACT NUMBER: (United States Howard Hughes Medical Institute)
SOURCE: PLoS ONE, (2008) Vol. 3, No. 5, pp. e2082. Electronic Publication: 2008-05-07.
Journal code: 101285081. E-ISSN: 1932-6203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200808
ENTRY DATE: Entered STN: 8 May 2008
Last Updated on STN: 29 Aug 2008
Entered Medline: 28 Aug 2008

AB Transient receptor potential (TRP) ion channels mediate key aspects of taste, smell, pain, temperature sensation, and pheromone detection. To deepen our understanding of TRP channel physiology, we require more diverse pharmacological tools. Citral, a bioactive component of lemongrass, is commonly used as a taste enhancer, as an odorant in perfumes, and as an insect repellent. Here we report that citral activates TRP channels found in sensory neurons (TRPV1 and TRPV3 , TRPM8, and TRPA1), and produces long-lasting inhibition of TRPV1-3 and TRPM8, while transiently blocking TRPV4 and TRPA1. Sustained citral inhibition is independent of internal calcium concentration, but is state-dependent, developing only after TRP channel opening. Citral's actions as a partial agonist are not due to cysteine modification of the channels nor are they a consequence of citral's stereoisoforms. The isolated aldehyde and alcohol cis and trans enantiomers (neral, nerol, geranial, and geraniol) each reproduce citral's actions. In juvenile rat dorsal root ganglion neurons, prolonged citral inhibition of native TRPV1 channels enabled the separation of TRPV2 and TRPV3 currents. We find that TRPV2 and TRPV3 channels are present in a high proportion of these neurons (94% respond to 2-aminoethyldiphenyl borate), consistent with our immunolabeling experiments and previous in situ hybridization studies. The TRPV1 activation requires residues in transmembrane segments two through four of the voltage-sensor domain, a region previously implicated in capsaicin activation of TRPV1 and analogous menthol activation of TRPM8. Citral's broad spectrum and prolonged sensory inhibition may prove more useful than capsaicin for allodynia, itch, or other types of pain involving superficial sensory nerves and skin.

L9 ANSWER 39 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2008152529 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18249134
TITLE: Investigation of TRPV1 loss-of-function phenotypes in transgenic shRNA expressing and knockout mice.
AUTHOR: Christoph Thomas; Bahrenberg Gregor; De Vry Jean; Englberger Werner; Erdmann Volker A; Frech Moritz; Kogel Babette; Rohl Thomas; Schiene Klaus; Schroder Wolfgang; Seibler Jost; Kurreck Jens
CORPORATE SOURCE: Preclinical Research and Development, Department of Pharmacology, Grunenthal, Zieglerstrasse 6, 52078 Aachen, Germany.. thomas.christoph@grunenthal.com
SOURCE: Molecular and cellular neurosciences, (2008 Mar) Vol. 37, No. 3, pp. 579-89. Electronic Publication: 2007-12-15. Journal code: 9100095. E-ISSN: 1095-9327.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200804
ENTRY DATE: Entered STN: 4 Mar 2008
Last Updated on STN: 11 Apr 2008
Entered Medline: 10 Apr 2008

AB The function of the transient receptor potential vanilloid 1 (TRPV1) cation channel was analyzed with RNA interference technologies and compared to TRPV1 knockout mice. Expression of shRNAs targeting TRPV1 in transgenic (tg) mice was proven by RNase protection assays, and TRPV1

downregulation was confirmed by reduced expression of TRPV1 mRNA and lack of receptor agonist binding in spinal cord membranes. Unexpectedly, TRPV3 mRNA expression was upregulated in shRNAtg but downregulated in knockout mice. Capsaicin-induced [Ca(2+)](i) changes in small diameter DRG neurons were significantly diminished in TRPV1 shRNAtg mice, and administration of capsaicin hardly induced hypothermia or nocifensive behaviour in vivo. Likewise, sensitivity towards noxious heat was reduced. Interestingly, spinal nerve injured TRPV1 knockout but not shRNAtg animals developed mechanical allodynia and hypersensitivity. The present study provides further evidence for the relevance of TRPV1 in neuropathic pain and characterizes RNA interference as valuable technique for drug target validation in pain research.

L9 ANSWER 40 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2007567810 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17850966
TITLE: Transient receptor potential V2 expressed in sensory neurons is activated by probenecid.
AUTHOR: Bang Sangsu; Kim Kyung Yoon; Yoo Sungjae; Lee Sang-Heon; Hwang Sun Wook
CORPORATE SOURCE: Korea University Graduate School of Medicine, Seoul 136-705, Republic of Korea.
SOURCE: Neuroscience letters, (2007 Sep 25) Vol. 425, No. 2, pp. 120-5. Electronic Publication: 2007-08-24.
Journal code: 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200712
ENTRY DATE: Entered STN: 25 Sep 2007
Last Updated on STN: 18 Dec 2007
Entered Medline: 14 Dec 2007
AB Temperature-activated transient receptor potential ion channels (thermoTRPs) are known to function as ambient temperature sensors and are also involved in peripheral pain sensation. The thermoTRPs are activated by a variety of chemicals, of which specific activators have been utilized to explore the physiology of particular channels and sensory nerve subtypes. The use of capsaicin for TRPV1 is an exemplary case for nociceptor studies. In contrast, specific agents for another vanilloid subtype channel, TRPV2 have been lacking. Here, we show that probenecid is able to activate TRPV2 using electrophysiological and calcium imaging techniques with TRPV2-expressing HEK293T cells. Five other sensory thermoTRPs-TRPV1, TRPV3, TRPV4, TRPM8 and TRPA1-failed to show a response to this drug in the same heterologous expression system, suggesting that probenecid is a specific activator for TRPV2. Probenecid-evoked responses were also reproduced in a distinct subset of cultured trigeminal neurons that were responsive to 2-aminoethoxydiphenyl borate, a TRPV1-3 activator. The probenecid-sensitive neurons were mainly distributed in a medium to large-diameter population, in agreement with previous observations with TRPV2 immunolocalization. Under inflammation, probenecid elicited nociceptive behaviors in in vivo assays. These results suggest that TRPV2 is specifically activated by probenecid and that this chemical might be useful for investigation of pain -related TRPV2 function.

L9 ANSWER 41 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2007456080 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17321113
TITLE: TRP channels: targets for the relief of pain.
AUTHOR: Levine Jon D; Alessandri-Haber Nicole

CORPORATE SOURCE: Department of Oral and Maxillofacial Surgery, Box 0440, University of California, San Francisco, 521 Parnassus Avenue, San Francisco, CA 94143-0440, USA.
SOURCE: Biochimica et biophysica acta, (2007 Aug) Vol. 1772, No. 8, pp. 989-1003. Electronic Publication: 2007-01-23. Ref: 192
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200709
ENTRY DATE: Entered STN: 7 Aug 2007
Last Updated on STN: 29 Sep 2007
Entered Medline: 28 Sep 2007

AB Patients with inflammatory or neuropathic pain experience hypersensitivity to mechanical, thermal and/or chemical stimuli. Given the diverse etiologies and molecular mechanisms of these pain syndromes, an approach to developing successful therapies may be to target ion channels that contribute to the detection of thermal, mechanical and chemical stimuli and promote the sensitization and activation of nociceptors. Transient Receptor Potential (TRP) channels have emerged as a family of evolutionarily conserved ligand-gated ion channels that contribute to the detection of physical stimuli. Six TRPs (TRPV1, TRPV2, TRPV3, TRPV4, TRPM8 and TRPA1) have been shown to be expressed in primary afferent nociceptors, pain sensing neurons, where they act as transducers for thermal, chemical and mechanical stimuli. This short review focuses on their contribution to pain hypersensitivity associated with peripheral inflammatory and neuropathic pain states.

L9 ANSWER 42 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2007361179 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17521436
TITLE: Differential expression of the capsaicin receptor TRPV1 and related novel receptors TRPV3, TRPV4 and TRPM8 in normal human tissues and changes in traumatic and diabetic neuropathy.
AUTHOR: Facer Paul; Casula Maria A; Smith Graham D; Benham Christopher D; Chessell Iain P; Bountra Chas; Sinisi Marco; Birch Rolfe; Anand Praveen
CORPORATE SOURCE: Peripheral Neuropathy Unit, Imperial College, Hammersmith Hospital, London, UK. p.facer@imperial.ac.uk. <p.facer@imperial.ac.uk>
SOURCE: BMC neurology, (2007) Vol. 7, pp. 11. Electronic Publication: 2007-05-23.
Journal code: 100968555. E-ISSN: 1471-2377.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200707
ENTRY DATE: Entered STN: 20 Jun 2007
Last Updated on STN: 11 Jul 2007
Entered Medline: 10 Jul 2007

AB BACKGROUND: Transient receptor potential (TRP) receptors expressed by primary sensory neurons mediate thermosensitivity, and may play a role in sensory pathophysiology. We previously reported that human dorsal root ganglion (DRG) sensory neurons co-expressed TRPV1 and TRPV3, and that these were increased in injured human DRG. Related receptors TRPV4, activated by warmth and eicosanoids, and TRPM8, activated by cool and menthol, have been characterised in pre-clinical models. However, the

role of TRPs in common clinical sensory neuropathies needs to be established. METHODS: We have studied TRPV1, TRPV3, TRPV4, and TRPM8 in nerves (n = 14) and skin from patients with nerve injury, avulsed dorsal root ganglia (DRG) (n = 11), injured spinal nerve roots (n = 9), diabetic neuropathy skin (n = 8), non-diabetic neuropathic nerve biopsies (n = 6), their respective control tissues, and human post mortem spinal cord, using immunohistological methods. RESULTS: TRPV1 and TRPV3 were significantly increased in injured brachial plexus nerves, and TRPV1 in hypersensitive skin after nerve repair, whilst TRPV4 was unchanged. TRPM8 was detected in a few medium diameter DRG neurons, and was unchanged in DRG after avulsion injury, but was reduced in axons and myelin in injured nerves. In diabetic neuropathy skin, TRPV1 expressing sub- and intra-epidermal fibres were decreased, as was expression in surviving fibres. TRPV1 was also decreased in non-diabetic neuropathic nerves. Immunoreactivity for TRPV3 was detected in basal keratinocytes, with a significant decrease of TRPV3 in diabetic skin. TRPV1-immunoreactive nerves were present in injured dorsal spinal roots and dorsal horn of control spinal cord, but not in ventral roots, while TRPV3 and TRPV4 were detected in spinal cord motor neurons. CONCLUSION: The accumulation of TRPV1 and TRPV3 in peripheral nerves after injury, in spared axons, matches our previously reported changes in avulsed DRG. Reduction of TRPV1 levels in nerve fibres in diabetic neuropathy skin may result from the known decrease of nerve growth factor (NGF) levels. The role of TRPs in keratinocytes is unknown, but a relationship to changes in NGF levels, which is produced by keratinocytes, deserves investigation. TRPV1 represents a more selective therapeutic target than other TRPs for pain and hypersensitivity, particularly in post-traumatic neuropathy.

L9 ANSWER 43 OF 52 MEDLINE on STN

ACCESSION NUMBER: 2006470744 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16829128
TITLE: More than cool: promiscuous relationships of menthol and other sensory compounds.
AUTHOR: Macpherson Lindsey J; Hwang Sun Wook; Miyamoto Takashi; Dubin Adrienne E; Patapoutian Ardem; Story Gina M
CORPORATE SOURCE: Department of Cell Biology, The Scripps Research Institute, La Jolla, CA 92037, USA.
CONTRACT NUMBER: NS046303 (United States NINDS)
NS047911 (United States NINDS)
NS04910 (United States NINDS)
SOURCE: Molecular and cellular neurosciences, (2006 Aug) Vol. 32, No. 4, pp. 335-43. Electronic Publication: 2006-07-07. Journal code: 9100095. ISSN: 1044-7431.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 9 Aug 2006
Last Updated on STN: 24 Oct 2006
Entered Medline: 24 Oct 2006
AB Several temperature-activated transient receptor potential (thermoTRP) ion channels are the molecular receptors of natural compounds that evoke thermal and pain sensations. Menthol, popularly known for its cooling effect, activates TRPM8--a cold-activated thermoTRP ion channel. However, human physiological studies demonstrate a paradoxical role of menthol in modulation of warm sensation, and here, we show that menthol also activates heat-activated TRPV3. We further show that menthol inhibits TRPA1, potentially explaining the use of menthol as an

analgesic. Similar to menthol, both camphor and cinnamaldehyde (initially reported to be specific activators of TRPV3 and TRPA1, respectively) also modulate other thermoTRPs. Therefore, we find that many "sensory compounds" presumed to be specific have a promiscuous relationship with thermoTRPs.

L9 ANSWER 44 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2006151454 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16540576
TITLE: Glial cell-line-derived neurotrophic factor expression in skin alters the mechanical sensitivity of cutaneous nociceptors.
AUTHOR: Albers Kathryn M; Woodbury C Jeffrey; Ritter Amy M; Davis Brian M; Koerber H Richard
CORPORATE SOURCE: Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15261, USA.
CONTRACT NUMBER: GM33730 (United States NIGMS)
NS23725 (United States NINDS)
NS31826 (United States NINDS)
NS33730 (United States NINDS)
SOURCE: The Journal of neuroscience : the official journal of the Society for Neuroscience, (2006 Mar 15) Vol. 26, No. 11, pp. 2981-90.
Journal code: 8102140. E-ISSN: 1529-2401.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200604
ENTRY DATE: Entered STN: 17 Mar 2006
Last Updated on STN: 22 Apr 2006
Entered Medline: 21 Apr 2006
AB Neurons classified as nociceptors are dependent on nerve growth factor (NGF) during embryonic development, but a large subpopulation lose this dependence during embryonic and postnatal times and become responsive to the transforming growth factor beta family member, glial cell line-derived growth factor (GDNF). To elucidate the functional properties of GDNF-dependent nociceptors and distinguish them from nociceptors that retain NGF dependence, the cellular and physiologic properties of sensory neurons of wild-type and transgenic mice that overexpress GDNF in the skin (GDNF-OE) were analyzed using a skin, nerve, dorsal root ganglion, and spinal cord preparation, immunolabeling, and reverse transcriptase-PCR assays. Although an increase in peripheral conduction velocity of C-fibers in GDNF-OE mice was measured, other electrophysiological properties, including resting membrane potential and somal action potentials, were unchanged. We also show that isolectin B4 (IB4)-positive neurons, many of which are responsive to GDNF, exhibited significantly lower thresholds to mechanical stimulation relative to wild-type neurons. However, no change was observed in heat thresholds for the same population of cells. The increase in mechanical sensitivity was found to correlate with significant increases in acid-sensing ion channels 2A and 2B and transient receptor potential channel A1, which are thought to contribute to detection of mechanical stimuli. These data indicate that enhanced expression of GDNF in the skin can change mechanical sensitivity of IB4-positive nociceptive afferents and that this may occur through enhanced expression of specific types of channel proteins.

L9 ANSWER 45 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2005539402 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16165301
TITLE: The TRPV1/2/3 activator 2-aminoethoxydiphenyl borate

sensitizes native nociceptive neurons to heat in wildtype but not TRPV1 deficient mice.
AUTHOR: Zimmermann K; Leffler A; Fischer M M J; Messlinger K; Nau C; Reeh P W
CORPORATE SOURCE: Department of Physiology and Pathophysiology, Friedrich-Alexander-University Erlangen-Nuremberg, Universitaetsstrasse 17, D-91054 Erlangen, Germany.. zimmermann@physiologie1.uni-erlangen.de
SOURCE: Neuroscience, (2005) Vol. 135, No. 4, pp. 1277-84. Electronic Publication: 2005-09-13. Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 12 Oct 2005
Last Updated on STN: 12 Jan 2006
Entered Medline: 11 Jan 2006

AB TRPV1 gene disruption results in a loss of capsaicin and proton responsiveness, but has minimal effects on heat-induced nocifensive behavior, suggesting that sensory transduction of heat is independent of TRPV1. TRPV3, another heat-activated ion channel but insensitive to capsaicin, was shown to be expressed in keratinocytes as well as in sensory neurons projecting to the skin. Recently, 2-aminoethoxydiphenyl borate was introduced as a TRPV3 agonist, but its selectivity was questioned by showing that it activated recombinant TRPV1 and TRPV2 as well. We used the isolated mouse skin-saphenous nerve preparation and whole-cell patch-clamping of cultured dorsal root ganglia neurons from TRPV1-/- and wildtype mice. We found no phenotypic differences between the heat responses of polymodal C-fibers, whereas cultured dorsal root ganglia neurons of TRPV1-/- hardly showed any heat-activated currents. Only C-fibers of wildtype but not TRPV1-/- mice were clearly sensitized to heat by 2-aminoethoxydiphenyl borate 10 and 100 microM; heat-activated current in wildtype neurons was only facilitated at 100 microM. Noxious heat-induced calcitonin gene-related peptide release showed clear deficits (<50%) in TRPV1 deficient skin, but the stimulated calcitonin gene-related peptide release from the isolated skull dura was unaffected. In both models, 2-aminoethoxydiphenyl borate was able to potentiate the heat response (46 degrees C, 5 min) in a concentration-dependent manner, again, only in wildtype but not TRPV1-/- mice, suggesting that TRPV2/3 are not involved in this sensitization to heat. The results further suggest that TRPV1 is not responsible for the normal heat response of native nociceptors but plays the essential role in thermal sensitization and a prominent one in controlling dermal calcitonin gene-related peptide release, i.e. neurogenic inflammation.

L9 ANSWER 46 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2005530487 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15952037
TITLE: TRPV channels as thermosensory receptors in epithelial cells.
AUTHOR: Lee Hyosang; Caterina Michael J
CORPORATE SOURCE: Departments of Biological Chemistry and Neuroscience, Johns Hopkins School of Medicine, 725 N Wolfe Street, Baltimore, MD 21205, USA.
SOURCE: Pflugers Archiv : European journal of physiology, (2005 Oct) Vol. 451, No. 1, pp. 160-7. Electronic Publication: 2005-06-11. Ref: 63
Journal code: 0154720. ISSN: 0031-6768.
PUB. COUNTRY: Germany: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200606
ENTRY DATE: Entered STN: 6 Oct 2005
Last Updated on STN: 7 Jun 2006
Entered Medline: 6 Jun 2006

AB Temperature-sensitive transient receptor potential vanilloid (TRPV) ion channels are critical contributors to normal pain and temperature sensation and therefore represent attractive targets for pain therapy. When these channels were first discovered, most attention was focused on their potential contributions to direct thermal activation of peripheral sensory neurons. However, recent anatomical, physiological, and behavioral studies have provided evidence that TRPV channels expressed in skin epithelial cells may also contribute to thermosensation in vitro and in vivo. Here, we review these studies and speculate on possible communication mechanisms from cutaneous epithelial cells to sensory neurons.

L9 ANSWER 47 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2004605623 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15578965
TITLE: Nociception and TRP Channels.
AUTHOR: Numazaki Mitsuko; Tominaga Makoto
CORPORATE SOURCE: Department of Anesthesiology, University of Tsukuba School of Medicine, Tsukuba 305-0006, Japan.
SOURCE: Current drug targets. CNS and neurological disorders, (2004 Dec) Vol. 3, No. 6, pp. 479-85. Ref: 95
Journal code: 101151150. ISSN: 1568-007X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 7 Dec 2004
Last Updated on STN: 24 Mar 2005
Entered Medline: 23 Mar 2005

AB Noxious thermal, mechanical, or chemical stimuli evoke pain through excitation of the peripheral terminals called nociceptor, and many kinds of ionotropic and metabotropic receptors are involved in this process. Capsaicin receptor TRPV1 is a nociceptor-specific ion channel that serves as the molecular target of capsaicin. TRPV1 can be activated not only by capsaicin but also by noxious heat (with a thermal threshold >43 degrees C) or protons (acidification), all of which are known to cause pain in vivo. Studies using TRPV1-deficient mice have shown that TRPV1 is essential for selective modalities of pain sensation and for thermal hyperalgesia. One mechanism underlying inflammatory pain which is initiated by tissue damage/inflammation and characterized by hypersensitivity is sensitization of TRPV1. In addition to TRPV1, there are five thermosensitive ion channels in mammals, all of which belong to the TRP (transient receptor potential) super family. These include TRPV2, TRPV3, TRPV4, TRPM8 and TRPA1. These channels exhibit distinct thermal activation thresholds (> 52 degrees C for TRPV2, > approximately 34-38 degrees C for TRPV3, > approximately 27-35 degrees C for TRPV4, < approximately 25-28 degrees C for TRPM8 and < 17 degrees C for TRPA1) and are expressed in primary sensory neurons as well as other tissues. Some of the thermosensitive TRP channels are likely to be involved in thermal nociception, since their activation thresholds are within the noxious range of temperatures.

L9 ANSWER 48 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2004497964 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15467255
TITLE: Molecular mechanisms of thermosensation.
AUTHOR: Tominaga Makoto
CORPORATE SOURCE: Section of Cell Signaling, Okazaki Institute for Integrative Bioscience, National Institutes of Natural Sciences, Okazaki, Aichi 444-8787, Japan.. tominaga@nips.ac.jp
SOURCE: Nippon yakurigaku zasshi. Folia pharmacologica Japonica, (2004 Oct) Vol. 124, No. 4, pp. 219-27. Ref: 50
Journal code: 0420550. ISSN: 0015-5691.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 7 Oct 2004
Last Updated on STN: 5 Jan 2005
Entered Medline: 4 Jan 2005
AB We feel a wide range of temperatures spanning from cold to heat. Within this range, temperatures over about 43 degrees C and below about 15 degrees C evoke not only a thermal sensation, but also a feeling of pain. In mammals, six thermosensitive ion channels have been reported, all of which belong to the TRP (transient receptor potential) super family. These include TRPV1 (VR1), TRPV2 (VRL-1), TRPV3, TRPV4, TRPM8 (CMR1), and TRPA1 (ANKTM1). These channels exhibit distinct thermal activation thresholds (>43 degrees C for TRPV1, >52 degrees C for TRPV2, >32-39 degrees C for TRPV3, >27-35 degrees C for TRPV4, <25-28 degrees C for TRPM8, and <17 degrees C for TRPA1) and are expressed in primary sensory neurons as well as other tissues. The involvement of TRPV1 in thermal nociception has been demonstrated by multiple methods, including the analysis of TRPV1-deficient mice. Temperature thresholds for activation of TRPV1, TRPV4, and TRPM8 are not fixed but changeable. Reduction of the temperature threshold for TRPV1 activation is thought to be one mechanism of inflammatory pain. Significant advances in thermosensation research have been made in the last several years with the cloning and characterization of thermosensitive TRP channels. With these clones in hand, we can begin to understand thermosensation from a molecular standpoint.

L9 ANSWER 49 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2004452923 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15362149
TITLE: Thermosensation and pain.
AUTHOR: Tominaga Makoto; Caterina Michael J
CORPORATE SOURCE: Section of Cell Signaling, Okazaki Institute for Integrative Bioscience, National Institutes of Natural Sciences, Okazaki 444-8787, Japan.. tominaga@nips.ac.jp
SOURCE: Journal of neurobiology, (2004 Oct) Vol. 61, No. 1, pp. 3-12. Ref: 80
Journal code: 0213640. ISSN: 0022-3034.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 14 Sep 2004

Last Updated on STN: 20 Dec 2004
Entered Medline: 13 Dec 2004

AB We feel a wide range of temperatures spanning from cold to heat. Within this range, temperatures over about 43 degrees C and below about 15 degrees C evoke not only a thermal sensation, but also a feeling of pain. In mammals, six thermosensitive ion channels have been reported, all of which belong to the TRP (transient receptor potential) superfamily. These include TRPV1 (VR1), TRPV2 (VRL-1), TRPV3, TRPV4, TRPM8 (CMR1), and TRPA1 (ANKTM1). These channels exhibit distinct thermal activation thresholds (>43 degrees C for TRPV1, >52 degrees C for TRPV2, > approximately 34-38 degrees C for TRPV3, > approximately 27-35 degrees C for TRPV4, < approximately 25-28 degrees C for TRPM8 and <17 degrees C for TRPA1), and are expressed in primary sensory neurons as well as other tissues. The involvement of TRPV1 in thermal nociception has been demonstrated by multiple methods, including the analysis of TRPV1-deficient mice. TRPV2, TRPM8, and TRPA1 are also very likely to be involved in thermal nociception, because their activation thresholds are within the noxious range of temperatures.

L9 ANSWER 50 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2004406460 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15194687
TITLE: 2-aminoethoxydiphenyl borate is a common activator of TRPV1, TRPV2, and TRPV3.
AUTHOR: Hu Hong-Zhen; Gu Qihai; Wang Chunbo; Colton Craig K; Tang Jisen; Kinoshita-Kawada Mariko; Lee Lu-Yuan; Wood Jackie D; Zhu Michael X
CORPORATE SOURCE: Department of Physiology and Cell Biology, The Ohio State University, Columbus Ohio 43210, USA.
CONTRACT NUMBER: DK057075 (United States NIDDK)
HL67379 (United States NHLBI)
NS42183 (United States NINDS)
SOURCE: The Journal of biological chemistry, (2004 Aug 20) Vol. 279, No. 34, pp. 35741-8. Electronic Publication: 2004-06-11.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 17 Aug 2004
Last Updated on STN: 16 Feb 2005
Entered Medline: 15 Feb 2005

AB The transient receptor potential (TRP) superfamily contains a large number of proteins encoding cation permeable channels that are further divided into TRPC (canonical), TRPM (melastatin), and TRPV (vanilloid) subfamilies. Among the six TRPV members, TRPV1, TRPV2, TRPV3, and TRPV4 form heat-activated cation channels, which serve diverse functions ranging from nociception to osmolality regulation. Although chemical activators for TRPV1 and TRPV4 are well documented, those for TRPV2 and TRPV3 are lacking. Here we show that in the absence of other stimuli, 2-aminoethoxydiphenyl borate (2APB) activates TRPV1, TRPV2, and TRPV3, but not TRPV4, TRPV5, and TRPV6 expressed in HEK293 cells. In contrast, 2APB inhibits the activity of TRPC6 and TRPM8 evoked by 1-oleolyl-2-acetyl-sn-glycerol and menthol, respectively. In addition, low levels of 2APB strongly potentiate the effect of capsaicin, protons, and heat on TRPV1 as well as that of heat on TRPV3 expressed in Xenopus oocytes. In dorsal root ganglia neurons, supra-additive stimulations were evoked by 2APB and capsaicin or 2APB and acid. Our data suggest the existence of a common activation mechanism for

TRPV1, TRPV2, and TRPV3 that may serve as a therapeutic target for pain management and treatment for diseases caused by hypersensitivity and temperature misregulation.

L9 ANSWER 51 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2004380255 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15283452
TITLE: The role of TRP channels in sensory neurons.
AUTHOR: Koltzenburg Martin
CORPORATE SOURCE: Neural Plasticity Unit, Institute of Child Health, 30 Guildford Street, London WC1N 1EH, UK.
SOURCE: Novartis Foundation symposium, (2004) Vol. 260, pp. 206-13; discussion 213-20, 277-9. Ref: 59
Journal code: 9807767. ISSN: 1528-2511.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 1 Aug 2004
Last Updated on STN: 7 Oct 2004
Entered Medline: 6 Oct 2004
AB Two parallel processes characterize the contemporary pain field. Firstly, enormous progress is being made in the discovery of the cellular and molecular mechanisms responsible for the pathogenesis of pain and secondly, there is a growing appreciation that multiple mechanisms contribute to common clinical pain syndromes. The aim of this chapter is to provide a short overview how transient receptor potential (TRP) channels could contribute to acute and chronic pain states. TRP channels of the vanilloid family (TRPV1, TRPV2, TRPV3 , TRPV4) are excited by heat stimuli whereas TRPM8 and ANKTM1 are cold responsive. TRPV1 and ANKTM1 are mediating the pungency of nociceptor-specific chemicals such as capsaicin or mustard oil. Sensitization of TRPV1 is an important mechanisms for heat hyperalgesia and thus the generation of chronic pain symptoms.

L9 ANSWER 52 OF 52 MEDLINE on STN
ACCESSION NUMBER: 2003295581 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12822433
TITLE: Molecular mechanisms of nociception and thermosensation: structures, expressions and functions of capsaicin receptor and its homologues.
AUTHOR: Numazaki Mitsuko; Tominaga Makoto
CORPORATE SOURCE: Mie University School of Medicine, Edobashi 2-174, Tsu, Mie 514-8507, Japan.
SOURCE: Seikagaku. The Journal of Japanese Biochemical Society, (2003 May) Vol. 75, No. 5, pp. 359-71. Ref: 92
Journal code: 0413564. ISSN: 0037-1017.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 26 Jun 2003
Last Updated on STN: 28 Sep 2003
Entered Medline: 26 Sep 2003

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                  enhanced
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                  Applications
 NEWS  7  OCT 24  CHEMLIST enhanced with intermediate list of
                  pre-registered REACH substances
 NEWS  8  NOV 21  CAS patent coverage to include exemplified prophetic
                  substances identified in English-, French-, German-,
                  and Japanese-language basic patents from 2004-present
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 NEWS 10  NOV 26  MEDLINE year-end processing temporarily halts
                  availability of new fully-indexed citations
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FULL ESTIMATED COST                                       0.21       0.21

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or hypertension or hypotension))
UNMATCHED LEFT PARENTHESIS 'AND ((PORTAL'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s ((pde or phosphodiesterase) (s) (five or V or 5)) and (portal (s) (pressure or
hypertension or hypotension))
L1 25 ((PDE OR PHOSPHODIESTERASE) (S) (FIVE OR V OR 5)) AND (PORTAL
(S) (PRESSURE OR HYPERTENSION OR HYPOTENSION))

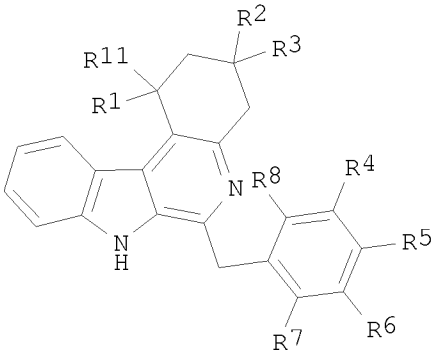
=> dup rem l1
PROCESSING COMPLETED FOR L1
L2 23 DUP REM L1 (2 DUPLICATES REMOVED)

=> d l2 ibib abs 1-23

L2 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:974175 CAPLUS
DOCUMENT NUMBER: 149:246509
TITLE: Preparation of
6-benzyl-2,3,4,7-tetrahydro-indolo[2,3-c]quinolines as
phosphodiesterase-5 (PDE5)
inhibitors
INVENTOR(S): Weinbrenner, Steffen; Dunkern, Torsten; Marx,
Degenhard; Schmidt, Beate; Stengel, Thomas; Flockerzi,
Dieter; Kautz, Ulrich; Hauser, Daniela; Diefenbach,
Joerg; Christiaans, Johannes A. M.; Menge, Wiro M. P.
B.
PATENT ASSIGNEE(S): Nycomed G.m.b.H., Germany
SOURCE: PCT Int. Appl., 81pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008095835	A1	20080814	WO 2008-EP51076	20080130
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1953159	A1	20080806	EP 2007-101742	20070205
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				

PRIORITY APPLN. INFO.: EP 2007-101742 A 20070205
OTHER SOURCE(S): MARPAT 149:246509
GI



I

AB Title compds. [I; R1 = H, OH; R11 = H; R1R11 = O; R2, R3 = H, alkyl; R4 = H, halo, alkoxy, NO2, amino; R5 = H, halo, alkyl, OH, alkoxy, NO2, amino, fluoromethoxy, etc.; R4R5 = OCH2O, OCH2CH2; R6-R8 = H, halo; with a specific exclusion], were prepared Thus, 3-hydroxy-2-(1H-indol-3-yl)-5,5-dimethylcyclohex-2-enone (preparation given) and 4-methoxyphenylacetic anhydride in MeNO2 were treated every 10 min. with HClO4 over 1 h followed by stirring for an addnl. 1 h to give 6-(4-methoxybenzylidene)-3,3-dimethyl-3,4,6,7-tetrahydro-2H-5-oxa-7-azabenzo[c]fluoren-1-one. The latter was microwaved with NH3 in MeCN at 130°C for 25 min. to give 6-(4-methoxybenzyl)-3,3-dimethyl-2,3,6,7-tetrahydroindolo[2,3-c]quinolin-1-one. The latter inhibited PDE5A1 activity with -log IC50 = 8.52.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:709127 CAPLUS
DOCUMENT NUMBER: 149:24920
TITLE: Method for treating a pulmonary arterial hypertension using ambrisentan
INVENTOR(S): Gerber, Michael J.; Dufton, Christopher
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080139593	A1	20080612	US 2007-953955	20071211
WO 2008073928	A1	20080619	WO 2007-US87058	20071211

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-869667P P 20061212

AB The present invention is based in part on a finding, in placebo-controlled clin. trials, that ambrisentan is effective for treatment of a pulmonary hypertension condition, more specifically pulmonary arterial hypertension (PAH), in subjects wherein the condition is relatively recently diagnosed. This method does not in any way negate ambrisentan therapy for subjects having a longer history of the condition. However, it recognizes that early intervention is advantageous. Benefits of the method to subjects having recent diagnosis (and poor prognosis without early intervention as exhibited, for example, in the NIH registry mentioned above) have now been quantified for the first time. PAH is associated with one or more of a congenital heart defect such as a systemic-to-pulmonary shunt or Eisenmenger 's syndrome, portal hypertension, use of a drug or toxin other than an anorexigen, thyroid disorder, glycogen storage disease, Gaucher disease, hereditary hemorrhagic telangiectasia, hemoglobinopathy, myeloproliferative disorder, splenectomy, pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis. Illustratively, in the placebo-controlled study described in Example 1 below, the median number of years for which PAH was present at baseline was 0.38 for subjects receiving placebo, 0.43 years for subjects receiving 2.5 mg ambrisentan daily, and 0.26 years for subjects receiving 5 mg ambrisentan daily. In the placebo-controlled study, the median number of years for which PAH was present at baseline was 0.54 for subjects receiving placebo, 0.33 years for subjects receiving 5 mg ambrisentan daily, and 0.60 years for subjects receiving 10 mg ambrisentan daily. The primary objective of this study was to determine the effect of ambrisentan on exercise capacity in subjects with PAH. The secondary objectives of this study were to evaluate effects of ambrisentan on other clin. measures of PAH, as well as safety and tolerability of the study drug.

L2 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:933691 CAPLUS

DOCUMENT NUMBER: 149:246505

TITLE: Preparation of 6-benzyl-2,3,4,7-tetrahydro-indolo[2,3-c]quinolines as phosphodiesterase-5 (PDE5) inhibitors

INVENTOR(S): Weinbrenner, Steffen; Dunkern, Torsten; Marx, Degenhard; Schmidt, Beate; Stengel, Thomas; Flockerzi, Dieter; Kautz, Ulrich; Hauser, Daniela; Diefenbach, Joerg; Christiaans, Johannes A. M.; Menge, Wiro M. P. B.

PATENT ASSIGNEE(S): Nycomed G.m.b.H., Germany

SOURCE: Eur. Pat. Appl., 47pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

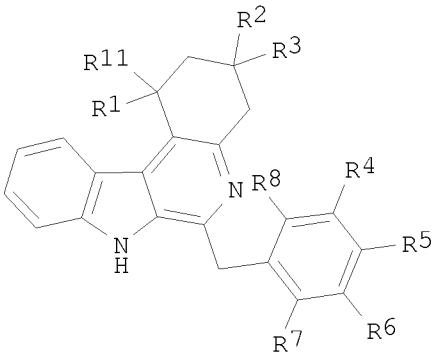
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1953159	A1	20080806	EP 2007-101742	20070205
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
WO 2008095835	A1	20080814	WO 2008-EP51076	20080130
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,				

CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,
FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.: EP 2007-101742 A 20070205
GI



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AB Title compds. [I; R1 = H, OH; R11 = H; R1R11 = O; R2, R3 = H, alkyl; R4 = H, halo, alkoxy, NO2, amino; R5 = H, halo, alkyl, OH, alkoxy, NO2, amino, fluoromethoxy, etc.; R4R5 = OCH2O, OCH2CH2; R6-R8 = H, halo; with a specific exclusion], were prepared Thus, 3-hydroxy-2-(1H-indol-3-yl)-5,5-dimethylcyclohex-2-enone (preparation given) and 4-methoxyphenylacetic anhydride in MeNO2 were treated every 10 min. with HClO4 over 1 h followed by stirring for an addnl. 1 h to give 6-(4-methoxybenzylidene)-3,3-dimethyl-3,4,6,7-tetrahydro-2H-5-oxa-7-azabenzo[c]fluoren-1-one. The latter was microwaved with NH3 in MeCN at 130°C for 25 min. to give 6-(4-methoxybenzyl)-3,3-dimethyl-2,3,6,7-tetrahydroindolo[2,3-c]quinolin-1-one. The latter inhibited PDE5A1 activity with -log IC50 = 8.52.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2008719174 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 18985812
TITLE: Sildenafil does not influence hepatic venous pressure gradient in patients with cirrhosis.
AUTHOR: Clemmesen Jens-Otto; Giraldi Annamaria; Ott Peter; Dalhoff Kim; Hansen Bent-Adel; Larsen Fin-Stolze
CORPORATE SOURCE: Department of Hepatology A-2121, Rigshospitalet, Blegdamsvej 9, Copenhagen DK-2100, Denmark.. otto.clemmesen@rh.regionh.dk
SOURCE: World journal of gastroenterology : WJG, (2008 Oct 28) Vol. 14, No. 40, pp. 6208-12.
Journal code: 100883448. ISSN: 1007-9327.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 6 Nov 2008
Last Updated on STN: 6 Nov 2008

AB AIM: To investigate if sildenafil increases splanchnic blood flow and changes the hepatic venous pressure gradient (HVPG) in patients with cirrhosis. Phosphodiesterase type-5 inhibitors are valuable in the treatment of erectile dysfunction and pulmonary hypertension in patients with end-stage liver disease. However, the effect of phosphodiesterase type-5 inhibitors on splanchnic blood flow and portal hypertension remains essentially unknown. METHODS: Ten patients with biopsy proven cirrhosis (five females/five males, mean age 54 +/- 8 years) and an HVPG above 12 mmHg were studied after informed consent. Measurement of splanchnic blood flow and the HVPG during liver vein catheterization were done before and 80 min after oral administration of 50 mg sildenafil. Blood flow was estimated by use of indocyanine green clearance technique and Fick's principle, with correction for non-steady state. RESULTS: The plasma concentration of sildenafil was 222 +/- 136 ng/mL 80 min after administration. Mean arterial blood pressure decreased from 77 +/- 7 mmHg to 66 +/- 12 mmHg, P = 0.003, while the splanchnic blood flow and oxygen consumption remained unchanged at 1.14 +/- 0.71 L/min and 2.3 +/- 0.6 mmol/min, respectively. Also the HVPG remained unchanged (18 +/- 2 mmHg vs 16 +/- 2 mmHg) with individual changes ranging from -8 mmHg to +2 mmHg. In seven patients, HVPG decreased and in three it increased. CONCLUSION: In spite of arterial blood pressure decreases 80 min after administration of the phosphodiesterase type-5 inhibitor sildenafil, the present study could not demonstrate any clinical relevant influence on splanichnic blood flow, oxygen consumption or the HVPG.

L2 ANSWER 5 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2008728916 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 18631254
TITLE: Acute administration of sildenafil enhances hepatic cyclic guanosine monophosphate production and reduces hepatic sinusoid resistance in cirrhotic patients.
AUTHOR: Lee Kuei-Chuan; Yang Ying-Ying; Wang Ying-Wen; Hou Ming-Chih; Lee Fa-Yauh; Lin Han-Chieh; Lee Shou-Dong
CORPORATE SOURCE: Division of Gastroenterology, Department of Gastroenterology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan.
SOURCE: Hepatology research : the official journal of the Japan Society of Hepatology, (2008 Dec) Vol. 38, No. 12, pp. 1186-93. Electronic Publication: 2008-07-04.
Journal code: 9711801. ISSN: 1386-6346.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED
ENTRY DATE: Entered STN: 13 Nov 2008
Last Updated on STN: 13 Nov 2008

AB Aim: In liver cirrhosis, the increased production of nitric oxide (NO) contributes to increased systemic and splanchnic vasodilatation. The inhibition of phosphodiesterase-5 (PDE-5), an enzyme responsible for the degradation of cyclic guanosine monophosphate (cGMP), is widely used in the treatment of erectile dysfunction. The aim of our study is to evaluate the overall effects of PDE-5 inhibitor administration on splanchnic, pulmonary and systemic hemodynamics in cirrhotic patients. Methods: Sildenafil, a specific PDE-5 inhibitor, was administrated orally to cirrhotic patients (n = 7) to see the hemodynamic changes. A control group receiving a placebo was used as a point of comparison (n = 6).

Results: Compared to the control group, the hepatic vein NO and cGMP levels were significantly increased after sildenafil administration in the sildenafil group (NO from 112.3 +/- 43.5 to 325.3 +/- 117.5 nM, P = 0.018; cGMP from 7.3 +/- 0.4 to 19.2 +/- 4.2 pmol, P = 0.018). The hepatic venous pressure gradient in the sildenafil group did not differ from that of the control group. However, a significantly decreased hepatic sinusoidal resistance in the sildenafil group (1999 +/- 1243 vs. 1563 +/- 1014 dyne/s/cm(-5), P < 0.05) was noted. The study also found that the right arterial pressure, mean pulmonary arterial pressure and pulmonary capillary wedge pressure were reduced at 60 min after administration, compared with the basal parameters in cirrhotic patients receiving sildenafil (RAP1.3 +/- 2.0 vs -0.6 +/- 1.3 mmHg, MPAP 14.1 +/- 11.3 vs 11.7 +/- 9.5 mmHg, PCWP 4.6 +/- 1.7 vs 2.9 +/- 1.6 mmHg, P < 0.05 respectively). Conclusions: An oral administration of 50 mg of sildenafil significantly decreased the mean pulmonary arterial pressure and hepatic sinusoid resistance with a significant increase in hepatic NO and cGMP production, and did not worsen portal hypertension in cirrhotic patients.

L2 ANSWER 6 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2008165128 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18280605
TITLE: Significant improvement of portopulmonary hypertension after 1-week terlipressin treatment.
AUTHOR: Kalambokis Georgios; Korantzopoulos Panagiotis; Nikas Spyros A; Theodorou Areti; Tsianos Epameinondas V
CORPORATE SOURCE: 1st Division of Internal Medicine, University of Ioannina, Medical School, 45110 Ioannina, Greece.
SOURCE: Journal of hepatology, (2008 Apr) Vol. 48, No. 4, pp. 678-80. Electronic Publication: 2008-01-28. Journal code: 8503886. ISSN: 0168-8278.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CASE REPORTS) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200808
ENTRY DATE: Entered STN: 8 Mar 2008 Last Updated on STN: 8 Aug 2008 Entered Medline: 7 Aug 2008
AB Cirrhosis associated with moderate and severe portopulmonary hypertension carries a poor prognosis. Optimal management has not yet been defined. Current treatment options, such as prostacyclin analogues, endothelin antagonists, and phosphodiesterase-5 inhibitors, are characterized by slow onset of action and various adverse effects, particularly in patients with advanced cirrhosis. Here, we report the significant reduction of pulmonary arterial pressure after 1-week terlipressin treatment in a patient with concomitant hepato-renal syndrome. Terlipressin could be a novel and safe treatment for portopulmonary hypertension.

L2 ANSWER 7 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2008117482 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18275769
TITLE: [Diagnosis and treatment of pulmonary hypertension]. Diagnostico y tratamiento de la hipertension pulmonar.
AUTHOR: Roman J Sanchez; Hernandez F J Garcia; Palma M J Castillo; Medina C Ocana
CORPORATE SOURCE: Unidad de Colagenosis e Hipertension Pulmonar, Servicio de Medicina Interna, Hospital Universitario Virgen del Rocio, Sevilla, Espana.
SOURCE: Revista clinica espanola, (2008 Mar) Vol. 208, No. 3, pp.

142-55. Ref: 71
Journal code: 8608576. ISSN: 0014-2565.
PUB. COUNTRY: Spain
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Spanish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200806
ENTRY DATE: Entered STN: 16 Feb 2008
Last Updated on STN: 24 Jun 2008
Entered Medline: 23 Jun 2008

AB Pulmonary arterial hypertension is an idiopathic process or can be associated with another circumstances (connective tissue diseases, congenital heart disease, portal hypertension, exposure to appetite suppressants or another drugs or infectious agents such as HIV). Most patients are diagnosed as the result of an evaluation of symptoms, whereas others are diagnosed incidentally or during screening of asymptomatic populations at risk. We reviews systematic screening for the approach to diagnosing pulmonary arterial hypertension. A diagnostic algorithm can guide the evaluation but it can be modified according to specific clinical circumstances. The number of therapeutic options has increased.in the last years. We reviews the use of calcium-channel blockers, prostacyclin (and analogues), endothelin-receptor antagonists, and phosphodiesterase-5 inhibitors, and the use of combination therapy, and provides specific recommendations about the actual treatment.

L2 ANSWER 8 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2007001493 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17197488
TITLE: PDE-5 inhibitors lower portal and pulmonary pressure in portopulmonary hypertension.
AUTHOR: Deibert P; Bremer H; Roessle M; Kurz-Schmieg A-K; Kreisel W
SOURCE: The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology, (2007 Jan) Vol. 29, No. 1, pp. 220-1.
Journal code: 8803460. ISSN: 0903-1936.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (CASE REPORTS)
Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200703
ENTRY DATE: Entered STN: 4 Jan 2007
Last Updated on STN: 24 Mar 2007
Entered Medline: 20 Mar 2007

L2 ANSWER 9 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2007497047 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17715635
TITLE: Hepatopulmonary syndrome and portopulmonary hypertension: what's new?.
AUTHOR: Colle Isabelle; Van Steenkiste Christophe; Geerts Anja; Van Vlierberghe Hans
CORPORATE SOURCE: Department of Hepatology and Gastroenterology, Ghent University Hospital, Ghent, Belgium..
Isabelle.Colle@ugent.be
SOURCE: Acta gastro-enterologica Belgica, (2007 Apr-Jun) Vol. 70, No. 2, pp. 203-9. Ref: 67

Journal code: 0414075. ISSN: 0001-5644.
PUB. COUNTRY: Belgium
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200710
ENTRY DATE: Entered STN: 25 Aug 2007
Last Updated on STN: 12 Oct 2007
Entered Medline: 11 Oct 2007

AB Hepatopulmonary syndrome (HPS) is found in 4-47% of patients with cirrhosis and is characterized by intrapulmonary vascular dilatations especially in the basal parts of the lung. Liver injury and/or portal hypertension trigger the release of endothelin-1, TNF-alpha, cytokines and mediate vascular shear stress and release of nitric oxide and carbon monoxide, all contributing to intrapulmonary vasodilation. Severe HPS increases mortality (30%) after liver transplantation, especially if Pa O2 is below 50 mmHg. The diagnosis is made by calculating the alveolar-arterial oxygen gradient and by performing a contrast echocardiography. Medical therapy fails and the only long-term treatment available is liver transplantation. More than 85% experience significant improvement or complete resolution in hypoxaemia, but this may take more than 1 year. Portopulmonary hypertension (PPHT) occurs in 2-8% of the patients with cirrhosis. Imbalance between vasodilating (decreased pulmonary expression of eNOS and prostacyclin I2) and vasoconstrictive agents (increased expression of ET-1 and angiotensin 1) may be responsible for misguided angiogenesis and pulmonary hypertension. The diagnosis is made by performing an echocardiography and a right heart catheterisation when systolic pulmonary artery pressure is higher than 30 mmHg on echocardiography. Although prostacyclin analogues are efficacious, adverse effects in terms of safety, tolerability and drug delivery occur. Bosentan is probably the therapy of choice for patients with PPHT because it decreases pulmonary but can also diminish portal hypertension.
Sildenafil, a phosphodiesterase-5 inhibitor is used for idiopathic pulmonary hypertension, however, it should be used cautiously in patients with portal hypertension as it may increase portal hypertension by splanchnic vasodilation.

L2 ANSWER 10 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2007523904 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 17623085
TITLE: Phosphodiesterase 5 inhibitors lower both portal and pulmonary pressure in portopulmonary hypertension: a case report.
AUTHOR: Bremer Hinrich C; Kreisel Wolfgang; Roecker Kai; Dreher Michael; Koenig Daniel; Kurz-Schmieg Anna Katharina; Blum Hubert E; Roessle Martin; Deibert Peter
CORPORATE SOURCE: Department of Gastroenterology, Hepatology, Endocrinology and Infectious Diseases, University Hospital, Freiburg, Germany.. wolfgang.kreisel@uniklinik-freiburg.de
SOURCE: Journal of medical case reports, (2007) Vol. 1, pp. 46. Electronic Publication: 2007-07-10.
Journal code: 101293382. E-ISSN: 1752-1947.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED
ENTRY DATE: Entered STN: 8 Sep 2007
Last Updated on STN: 8 Dec 2007

AB ABSTRACT: BACKGROUND: Portopulmonary hypertension (PPHTN) is a severe

complication in liver cirrhosis. PDE5 inhibitors lower pulmonary arterial pressure (PAP) in PPHTN. However, their effect on portal hypertension has not yet been investigated. CASE PRESENTATION: A 55 year old male patient presented with PPHTN and alcoholic liver cirrhosis. 10 mg of Tadalafil, a PDE5 inhibitor with a long half-life, was administered orally under continuous monitoring of pulmonary and portal hemodynamics. For maintenance therapy the patient received Sildenafil 20 mg bid.Tadalafil lowered mean PAP from 45 to 39 mmHg within 60 minutes. Cardiac output (CO) increased from 6.8 to 7.9 l/min. Central venous pressure (CVP) remained stable at 3 mmHg. Systolic and diastolic blood pressure was lowered from 167/89 to 159/86 mmHg. Pulse rate increased from 75 to 87 per min. Wedged hepatic vein pressure (WHVP) decreased from 21 to 18 mm Hg, hepatovenous pressure gradient (HVPG) decreased from 10 to 7 mmHg. Hemodynamic monitoring after 6 months of Sildenafil therapy revealed a sustained lowering of mean PAP. HVPG remained constant at 10 mmHg. Cardiac and pulmonary performance had further improved. CONCLUSION: This case report shows for the first time, that phosphodiesterase 5 inhibitors lower both portal and pulmonary pressure in portopulmonary hypertension.

L2 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1123280 CAPLUS
DOCUMENT NUMBER: 145:449221
TITLE: Roflumilast and roflumilast N-oxide for the treatment of pulmonary hypertension, and combinations with phosphodiesterase 5 inhibitors
INVENTOR(S): Beume, Rolf; Hatzelmann, Armin; Marx, Degenhard; Schudt, Christian; Tenor, Hermann; Eddahibi, Saadia; Adnot, Serge
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 40pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006111495	A1	20061026	WO 2006-EP61557	20060412
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006237300	A1	20061026	AU 2006-237300	20060412
CA 2604295	A1	20061026	CA 2006-2604295	20060412
EP 1874309	A1	20080109	EP 2006-725734	20060412
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008536888	T	20080911	JP 2008-507056	20060412
MX 200712711	A	20080111	MX 2007-12711	20071012
CN 101163476	A	20080416	CN 2006-80013022	20071018
NO 2007005662	A	20071107	NO 2007-5662	20071107

IN 2007MN01889	A	20071207	IN 2007-MN1889		20071112
KR 2008002950	A	20080104	KR 2007-726282		20071112
PRIORITY APPLN. INFO.:			EP 2005-103147	A	20050419
			WO 2006-EP61557	W	20060412

AB The invention discloses the use of roflumilast, roflumilast-N-Oxide, or a pharmaceutically acceptable salt of either for the treatment of pulmonary hypertension. The invention addnl. discloses the use of roflumilast, roflumilast-N-oxide or a pharmaceutically acceptable salt of either in combination with a phosphodiesterase 5 inhibitor, or a pharmaceutically acceptable salt thereof, for the treatment of pulmonary hypertension.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:978593 CAPLUS
DOCUMENT NUMBER: 145:348634
TITLE: Organic nitric oxide enhancing salts of angiotensin II antagonists, compositions and methods of use
INVENTOR(S): Garvey, David, S.; Cai, Xiong; Lin, Chia-En; Ranatunge, Ramini, R.; Stevenson, Cheri, A.; Wey, Shiow-Jyi
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 126pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006099058	A2	20060921	WO 2006-US8441	20060309
WO 2006099058	A3	20070518		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2006223392	A1	20060921	AU 2006-223392	20060309
CA 2597444	A1	20060921	CA 2006-2597444	20060309
EP 1861093	A2	20071205	EP 2006-737602	20060309
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008533031	T	20080821	JP 2008-500923	20060309
PRIORITY APPLN. INFO.:			US 2005-659401P	P 20050309
			US 2005-750773P	P 20051215
			WO 2006-US8441	W 20060309

OTHER SOURCE(S): MARPAT 145:348634

AB The invention describes compns. and kits comprising at least one organic nitric oxide enhancing salt of an angiotensin II antagonist, and, optionally, at least one nitric oxide enhancing compound and/or at least one therapeutic agent. The invention also provides methods for (a) treating cardiovascular diseases; (b) treating renovascular diseases; (c) treating

diabetes; (d) treating diseases resulting from oxidative stress; (e) treating endothelial dysfunctions; (f) treating diseases caused by endothelial dysfunctions; (g) treating cirrhosis; (h) treating pre-eclampsia; (j) treating osteoporosis; (k) treating nephropathy; (1) treating peripheral vascular diseases; (m) treating portal hypertension; (n) treating ophthalmic disorders; (o) treating metabolic syndrome; and (p) treating hyperlipidemia. The organic nitric oxide enhancing compds. that form salts with the angiotensin II antagonists are organic nitrates, organic nitrites, nitrosothiols, thionitrites, thionitrates, NONOates, heterocyclic nitric oxide donors and/or nitroxides. The heterocyclic nitric oxide donors are furoxans, sydnonimines, oxatriazole-5-ones and/or oxatriazole-5-imines.

L2 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:149404 CAPLUS
DOCUMENT NUMBER: 144:205821
TITLE: 2-Phenyl-substituted imidazotriazinone derivative phosphodiesterase 5 inhibitors for the treatment of symptoms treatable by increasing cGMP levels
INVENTOR(S): Haning, Helmut
PATENT ASSIGNEE(S): Bayer Healthcare A.-G., Germany
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006015715	A1	20060216	WO 2005-EP8057	20050723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
DE 102004038328	A1	20060316	DE 2004-102004038328	20040806
AU 2005270446	A1	20060216	AU 2005-270446	20050723
CA 2575907	A1	20060216	CA 2005-2575907	20050723
EP 1776120	A1	20070425	EP 2005-764196	20050723
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				
CN 101035539	A	20070912	CN 2005-80034023	20050723
JP 2008509101	T	20080327	JP 2007-524224	20050723
BR 2005014123	A	20080527	BR 2005-14123	20050723
IN 2007DN01126	A	20070427	IN 2007-DN1126	20070212
KR 2007041613	A	20070418	KR 2007-705245	20070305
NO 2007001231	A	20070503	NO 2007-1231	20070306
US 20070299088	A1	20071227	US 2007-659624	20070905
PRIORITY APPLN. INFO.:			DE 2004-102004038328A	20040806
			WO 2005-EP8057 W	20050723

OTHER SOURCE(S): MARPAT 144:205821
AB The invention relates to the use of PDE 5 inhibitors,

and especially of known 2-phenyl-substituted imidazotriazinone derivs., for producing medicaments for the treatment of symptoms that can be treated by increasing cGMP levels in certain tissues, e.g. acute myocardial infarction and damage caused by reperfusion, various symptoms in the female and male reproductive system and urogenital tract, gastrointestinal diseases, damage caused by diabetes, and liver failure.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2006614048 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17048047
TITLE: Portopulmonary hypertension.
AUTHOR: Halank Michael; Ewert Ralf; Seyfarth Hans-Juergen; Hoeffken Gert
CORPORATE SOURCE: Carl Gustav Carus University Dresden, Internal Medicine I, Fetscherstr. 74, 01307 Dresden, Germany.
SOURCE: Journal of gastroenterology, (2006 Sep) Vol. 41, No. 9, pp. 837-47. Ref: 86
Journal code: 9430794. ISSN: 0944-1174.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200701
ENTRY DATE: Entered STN: 19 Oct 2006
Last Updated on STN: 10 Jan 2007
Entered Medline: 9 Jan 2007
AB Portopulmonary hypertension (PPHT) is defined as precapillary pulmonary hypertension accompanied by hepatic disease or portal hypertension. Pulmonary hypertension results from excessive pulmonary vascular remodeling and vasoconstriction. These histological alterations have been indistinguishable from those of other forms of pulmonary arterial hypertension. Factors involved in the pathogenesis of PPHT include volume overload, hyperdynamic circulation, and circulating vasoactive mediators. The disorder has a substantial impact on survival and requires focused treatment. Liver transplantation in patients with moderate to severe PPHT is associated with a significantly reduced survival rate. The best medical treatment for patients with PPHT is controversial; most authors currently regard continuous intravenous application of prostacyclin as the treatment of choice for patients with severe PPHT. There is only very limited reported experience with inhaled prostacyclin or its analog, iloprost. Increasing evidence of the efficacy of the endothelin-receptor antagonist bosentan and of the phosphodiesterase-5 inhibitor sildenafil is emerging in highly selected patients with PPHT. In the future, a combination therapy of the above-mentioned agents might become a therapeutic option. Other agents such as beta-blockers seem to be harmful to patients with moderate to severe portopulmonary hypertension. Up-to-date, randomized, double-blind, controlled clinical trials are lacking and are needed urgently.

L2 ANSWER 15 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2006007040 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16393289
TITLE: Effect of vardenafil, an inhibitor of phosphodiesterase-5, on portal haemodynamics in normal and cirrhotic liver -- results of a pilot study.
AUTHOR: Deibert P; Schumacher Y-O; Ruecker G; Opitz O G; Blum H E; Rossle M; Kreisel W

CORPORATE SOURCE: Department of Preventive and Rehabilitative Sports Medicine, University Hospital Freiburg, Freiburg, Germany.
SOURCE: Alimentary pharmacology & therapeutics, (2006 Jan 1) Vol. 23, No. 1, pp. 121-8.
Journal code: 8707234. ISSN: 0269-2813.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200605
ENTRY DATE: Entered STN: 6 Jan 2006
Last Updated on STN: 4 May 2006
Entered Medline: 3 May 2006

AB BACKGROUND: Dysregulation of the cyclic guanosine 3',5' monophosphate-nitric oxide system is in part responsible for portal hypertension in cirrhosis. AIM: To test the effects of inhibitors of phosphodiesterase-5 on portal haemodynamics. METHODS: To 18 healthy subjects and 18 patients with Child A liver cirrhosis, 10 mg of vardenafil, an inhibitor of phosphodiesterase-5, were administered orally. Doppler sonographic measurements of hepatic and splanchnic blood flow, systemic blood pressure and heart rate were recorded before, 1 h after, and 48 h after the application. Vardenafil plasma levels were determined after 1 h. In five patients, invasive registration of free and wedged hepatic vein pressure was performed. RESULTS: Portal venous flow increased in patients from 0.82 +/- 0.30 L/min (mean +/- s.d.) by 26% (CI: 16-37%, P = 0.0004) and in healthy subjects from 0.75 +/- 0.20 L/min (mean +/- s.d.) by 19% (CI: 9-28%; P = 0.0010). Celiac and hepatic artery resistivity indices rose significantly. Systemic blood pressure decreased slightly in patients. The wedged hepatic venous pressure gradient decreased in four of five patients with liver cirrhosis. Vardenafil plasma levels were higher in patients (14 +/- 10 microg/L) than in healthy subjects (9 +/- 6 microg/L; n.s.). CONCLUSIONS: Inhibition of phosphodiesterase-5 increases portal flow and lowers portal pressure by a decrease in sinusoidal resistance and may be a novel therapeutic strategy for portal hypertension.

L2 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1303561 CAPLUS
DOCUMENT NUMBER: 144:285886
TITLE: Bosentan for the treatment of pulmonary arterial hypertension. (II)
AUTHOR(S): Antoniu, Sabina A.
CORPORATE SOURCE: Clinic of Pulmonary Disease, University of Medicine and Pharmacy, Iasi, 700070, Rom.
SOURCE: Therapy (2005), 2(6), 849-852
CODEN: THERCR; ISSN: 1475-0708
PUBLISHER: Future Drugs Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Portopulmonary hypertension is defined as pulmonary arterial hypertension occurring in the presence of portal hypertension. It is classified as a subset of pulmonary arterial hypertension and accordingly it is defined hemodynamically. Portopulmonary hypertension shares the main pathol. features as well as diagnostic approach with other forms of pulmonary arterial hypertension. Several nonpharmacol. and pharmacol. approaches are currently available. Among the pharmacol. approaches prostacycline and its derivs., phosphodiesterase-5 inhibitors such as sildenafil and endothelin receptor antagonists such as bosentan, have been used in portopulmonary hypertension treatment. This is a case series report on

the long-term efficacy of bosentan treatment for severe (New York Heart Association functional Class III and IV) portopulmonary hypertension.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2005615688 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16294183
TITLE: [Pulmonary arterial hypertension]. Hypertension arterielle pulmonaire.
AUTHOR: Montani D; Jais X; Sitbon O; Capron F; Simonneau G; Humbert M
CORPORATE SOURCE: Centre des Maladies Vasculaires Pulmonaires, UPRES EA2705, Service de Pneumologie et Reanimation respiratoire, Hopital Antoine-Beclere, Universite Paris-Sud, Assistance Publique, Hopitaux de Paris, Clamart, France.
SOURCE: Revue des maladies respiratoires, (2005 Sep) Vol. 22, No. 4, pp. 651-66. Ref: 59
Journal code: 8408032. ISSN: 0761-8425.
PUB. COUNTRY: France
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 22 Nov 2005
Last Updated on STN: 24 Dec 2005
Entered Medline: 23 Dec 2005
AB INTRODUCTION: Pulmonary arterial hypertension (PAH) is a rare condition characterised by progressively elevated pulmonary arterial resistance leading to right heart failure. STATE OF THE ART: A recent classification distinguishes idiopathic PAH, familial PAH and PAH secondary to other conditions (connective tissue disease, congenital heart disease, portal hypertension, human immunodeficiency virus infection or appetite suppressant exposure). Echocardiography is the initial investigation of choice for non-invasive detection of PAH but measurement of pulmonary pressures and cardiac output during right-heart catheterization are necessary to confirm the diagnosis of PAH. Conventional treatment includes non-specific drugs (warfarin, diuretics, oxygen). Intravenous epoprostenol is the first-line treatment for the most severely affected patients. In less severe cases, the first-line treatment may include bosentan or a prostacyclin analogue. PERSPECTIVES AND CONCLUSIONS: Recent advances in the management of PAH have markedly improved prognosis. The avai-lability of novel specific drugs including type 5 phosphodiesterase inhibitors offers novel therapeutic perspectives but their exact role in the treatment of PAH is still uncertain. The evolution of therapy from vasodilators to antiproliferative agents reflects the advancement in our understanding of the mechanisms mediating pulmonary arterial hypertension.

L2 ANSWER 18 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2005078879 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15708146
TITLE: Fatal variceal rupture after sildenafil use: report of a case.
AUTHOR: Finley David S; Lugo Brian; Ridgway James; Teng Wang; Imagawa David K
CORPORATE SOURCE: Division of Hepatobiliary and Pancreas Surgery, Department of Surgery, University of California, Irvine, Orange, California 92868, USA.. finds@uci.edu
SOURCE: Current surgery, (2005 Jan-Feb) Vol. 62, No. 1, pp. 55-6.

Journal code: 7802123. ISSN: 0149-7944.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 16 Feb 2005
Last Updated on STN: 24 Jun 2005
Entered Medline: 23 Jun 2005

AB Sildenafil may increase the risk of variceal bleeding in portal hyptertension by increasing splanchnic blood flow. We report herein the second case of variceal rupture after sildenafil use.

L2 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:1080763 CAPLUS
DOCUMENT NUMBER: 142:16820
TITLE: Use of a phosphodiesterase V inhibitor for the prophylaxis and/or treatment of portal hypertension
INVENTOR(S): Kreisel, Wolfgang
PATENT ASSIGNEE(S): Universitatsklinikum Freiburg, Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108062	A2	20041216	WO 2004-EP6014	20040603
WO 2004108062	A3	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10325813	A1	20050105	DE 2003-10325813	20030606
DE 10325813	B4	20071220		
EP 1635838	A2	20060322	EP 2004-739573	20040603
EP 1635838	B1	20070502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1871010	A	20061129	CN 2004-80022512	20040603
JP 2006527177	T	20061130	JP 2006-508268	20040603
AT 361074	T	20070515	AT 2004-739573	20040603
ES 2287740	T3	20071216	ES 2004-739573	20040603
EP 1923073	A2	20080521	EP 2006-25229	20040603
EP 1923073	A3	20080709		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
KR 2006031614	A	20060412	KR 2005-723300	20051205
US 20070004744	A1	20070104	US 2006-559694	20060501

PRIORITY APPLN. INFO.: DE 2003-10325813 A 20030606
EP 2004-739573 A3 20040603

WO 2004-EP6014 W 20040603

AB The invention discloses a medicament for the prophylaxis and/or treatment of diseases or complications associated with portal hypertension, especially hemorrhagic complications. The invention uses a phosphodiesterase V inhibitor, e.g. sildenafil.

L2 ANSWER 20 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2004573302 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15545947
TITLE: [Pulmonary hypertension: from genetics to treatments]. Hypertension arterielle pulmonaire: de la genetique aux traitements.
AUTHOR: Humbert M; Yaici A; Sztrymf B; Montani D
CORPORATE SOURCE: Service de Pneumologie et Reanimation Respiratoire, Centre des Maladies Vasculaires Pulmonaires, UPRES EA 2705, Reseau INSERM-AFM sur l'hypertension arterielle pulmonaire, Hopital Antoine-Beclere, Clamart.. humbert@ipsc.u-psud.fr
SOURCE: Revue de pneumologie clinique, (2004 Sep) Vol. 60, No. 4, pp. 196-201. Ref: 30
Journal code: 8406312. ISSN: 0761-8417.
PUB. COUNTRY: France
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 17 Nov 2004
Last Updated on STN: 18 May 2005
Entered Medline: 17 May 2005

AB Pulmonary hypertertension (PHT) is a rare disease defined by increased resistance of the pulmonary arteries inevitably leading to right heart failure if specific treatment is not given. This disease can occur sporadically (idiopathic or primary PHT), within a familial context (familial PHT, BMPR2 gene mutation), or occur as a complication of other diseases (connective tissue disease, congenital cardiomyopathy, human immunodeficiency virus infection, portal hypertension, use of anorexigenic agents). The incidence of primary PHT is 2 million cases per year, probably an underestimation due to the low specificity of clinical signs, predominantly exercise-induced dyspnea. Recent therapeutic advances (prostacyclin and endothelin receptor antagonists administered in continuous infusion) have improved the prognosis of this orphan disease. Inhaled iloprost and type 5 phosphodiesterase inhibitors should be evaluated for this indication. Lung transplantation is reserved for patients unresponsive to medical treatment.

L2 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:313030 CAPLUS
DOCUMENT NUMBER: 140:332199
TITLE: Systemic and splanchnic haemodynamic effects of sildenafil in an in vivo animal model of cirrhosis support for a risk in cirrhotic patients
AUTHOR(S): Colle, Isabelle; De Vriese, An S.; Van Vlierberghe, Hans; Lameire, Norbert H.; DeVos, Martine
CORPORATE SOURCE: Division of Hepato-Gatroenterology, Ghent University Hospital, Ghent, Belg.
SOURCE: Liver International (2004), 24(1), 63-68
CODEN: LIINCM; ISSN: 1478-3223
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objectives: Sildenafil is a selective inhibitor of the cGMP-specific phosphodiesterase type V (PDE-V) in the corpus cavernosum. PDE-V is also present in the mesenteric artery. Cirrhosis is complicated by a splanchnic vasodilation attributed to a local overprodn. of nitric oxide (NO). As sildenafil potentiates the effects of NO, it may further decrease mesenteric vascular tone and increase portal venous blood flow. The aim is to evaluate the effects of sildenafil on the systemic and splanchnic hemodynamics in an exptl. model of cirrhosis. Methods: Secondary biliary cirrhosis was induced in male Wistar rats by common bile duct ligation (CBDL, n = 8); control rats were sham-operated (sham, n = 7). The mean arterial pressure (MAP), portal venous pressure (PVP) and arterial mesenteric blood flow (MBF) were measured after intramesenteric (0.01 - 10 mg/kg) and after i.v. (0.01 - 10 mg/kg) administration of sildenafil. Results: Baseline PVP was significantly higher in CBDL than in sham rats, whereas baseline MAP tended to be lower and MBF tended to be higher in CBDL compared with sham rats. Both intramesenteric and i.v. injection of sildenafil significantly decreased MAP and increased MBF and PVP in a dose-dependent way. The decrease in MAP was significantly less important in CBDL than in sham rats. The increase in MBF was importantly lower in CBDL than in sham rats. PVP tended to increase more significantly in sham rats than in CBDL. Conclusion: Sildenafil increases MBF and PVP and induces systemic hypotension. The effects are less pronounced in cirrhosis, suggesting vascular hyporesponsiveness to sildenafil. Although the rise in PVP in cirrhotic animals is smaller than in controls, it may present a risk for hemorrhagic complications. Further studies are necessary before prescribing sildenafil to patients with cirrhosis.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 22 OF 23 MEDLINE on STN

ACCESSION NUMBER: 2004156325 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15049592
TITLE: [Pulmonary arterial hypertension]. Hypertension arterielle pulmonaire.
AUTHOR: Montani David; Hamid Abdul; Yaici Azzedine; Sztrymf Benjamin; Humbert Marc
CORPORATE SOURCE: Centre des maladies vasculaires pulmonaires, UPRES EA2705, service de pneumologie et reanimation respiratoire, hopital Antoine Beclere, 92140 Clamart.
SOURCE: La Revue du praticien, (2004 Jan 15) Vol. 54, No. 1, pp. 5-13. Ref: 23
Journal code: 0404334. ISSN: 0035-2640.
PUB. COUNTRY: France
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 31 Mar 2004
Last Updated on STN: 22 Sep 2004
Entered Medline: 21 Sep 2004

AB Pulmonary arterial hypertension (PAH) is a rare condition characterised by elevated pulmonary arterial resistance leading to right heart failure. PAH can be sporadic (idiopathic PAH, or primary pulmonary hypertension), familial (caused by germline BMPR2 mutations, a type II member of the TGFbeta receptor superfamily), or related to other conditions including connective tissue disease, congenital heart disease, human immunodeficiency virus infection, portal hypertension, appetite suppressant exposure... Idiopathic PAH has

a prevalence of 2 per million per year in France. The lack of specificity of PAH symptoms (mostly dyspnea) presumably lead to underdiagnosis of this condition. Echocardiography is the investigation of choice for non-invasive screening. Measurement of hemodynamic parameters during right-heart catheterism is mandatory to establish the diagnosis (mean pulmonary artery pressure >25 mmHg and pulmonary artery wedge pressure <12 mmHg). Acute pulmonary vasodilator testing should be performed with nitric oxide or prostacyclin during right-heart catheterization. Recent advances in the management of PAH including continuous intravenous prostacyclin infusion and endothelin receptor antagonists have improved markedly the patients' prognosis. Novel treatments such as inhaled iloprost and type 5 phosphodiesterase inhibitors have to be further evaluated in this setting. Lung transplantation is the last option for patients deteriorating despite medical treatment.

L2 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 1995:396408 CAPLUS
DOCUMENT NUMBER: 122:157633
ORIGINAL REFERENCE NO.: 122:29029a,29032a
TITLE: Change in vascular cAMP and cGMP contents in portal hypertensive rats
AUTHOR(S): Huang, Yi-Tsau; Lo, Jeng-Wu; Lin, Han-Chieh; Tsai, Yang-Te; Hong, Chaung-Ye; Yang, May C. M.
CORPORATE SOURCE: Institute Traditional Medicine, National Yang Ming Medical College, Taipei, Taiwan
SOURCE: Pharmacology (1995), 50(2), 86-91
CODEN: PHMGBN; ISSN: 0031-7012
PUBLISHER: Karger
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to investigate the possible changes of cyclic nucleotide contents in portal hypertensive rats. Portal hypertension was induced by partial portal vein ligation (PVL) in Sprague-Dawley rats. Sham-operated rats served as controls. Hemodynamic and cyclic nucleotide measurements were performed at 14 days after surgery. The portal venous pressure was significantly higher, while systemic arterial pressure and heart rate were lower in PVL rats than those in controls. Basal cAMP (PVL, 10.91 ± 0.98, vs. sham, 8.08 ± 0.81 pmol/mg protein) and cGMP (PVL, 0.91 ± 0.12, vs. sham, 0.59 ± 0.05 pmol/mg protein) contents in the tail artery were significantly higher in PVL rats. Isobutyryl methylxanthine (10-5 M), a nonspecific phosphodiesterase inhibitor, exerted similarly stimulating effects on the tissue cAMP (PVL, 158 ± 10, vs. sham, 178 ± 20%) and cGMP (295 ± 28 vs. 316 ± 71%) levels in both PVL and control rats; so did forskolin (10-6 M) on the cAMP (184 ± 20 vs. 197 ± 66%) content in both groups. Our results showed that the arterial cAMP and cGMP contents were higher in PVL rats, which may contribute to the reduction of peripheral resistance in portal hypertension.

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 NEWS  3  OCT 07  EPFULL enhanced with full implementation of EPC2000
 NEWS  4  OCT 07  Multiple databases enhanced for more flexible patent
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 NEWS  5  OCT 22  Current-awareness alert (SDI) setup and editing
                  enhanced
 NEWS  6  OCT 22  WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT
                  Applications
 NEWS  7  OCT 24  CHEMLIST enhanced with intermediate list of
                  pre-registered REACH substances
 NEWS  8  NOV 21  CAS patent coverage to include exemplified prophetic
                  substances identified in English-, French-, German-,
                  and Japanese-language basic patents from 2004-present
 NEWS  9  NOV 26  MARPAT enhanced with FSORT command
 NEWS 10  NOV 26  MEDLINE year-end processing temporarily halts
                  availability of new fully-indexed citations
 NEWS 11  NOV 26  CHEMSAFE now available on STN Easy
 NEWS 12  NOV 26  Two new SET commands increase convenience of STN
                  searching
 NEWS 13  DEC 01  ChemPort single article sales feature unavailable

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              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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L1 9 PORTOPULMONAR? AND (PDE OR PHOSPHODIESTERASE) AND (FIVE OR V OR 5)

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L1 ANSWER 1 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2008165128 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18280605
TITLE: Significant improvement of portopulmonary hypertension after 1-week terlipressin treatment.
AUTHOR: Kalambokis Georgios; Korantzopoulos Panagiotis; Nikas Spyros A; Theodorou Areti; Tsianos Epameinondas V
CORPORATE SOURCE: 1st Division of Internal Medicine, University of Ioannina, Medical School, 45110 Ioannina, Greece.
SOURCE: Journal of hepatology, (2008 Apr) Vol. 48, No. 4, pp. 678-80. Electronic Publication: 2008-01-28.
Journal code: 8503886. ISSN: 0168-8278.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200808
ENTRY DATE: Entered STN: 8 Mar 2008
Last Updated on STN: 8 Aug 2008
Entered Medline: 7 Aug 2008
AB Cirrhosis associated with moderate and severe portopulmonary hypertension carries a poor prognosis. Optimal management has not yet been defined. Current treatment options, such as prostacyclin analogues, endothelin antagonists, and phosphodiesterase-5 inhibitors, are characterized by slow onset of action and various adverse effects, particularly in patients with advanced cirrhosis. Here, we report the significant reduction of pulmonary arterial pressure after 1-week terlipressin treatment in a patient with concomitant hepato-renal syndrome. Terlipressin could be a novel and safe treatment for portopulmonary hypertension.

L1 ANSWER 2 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2007523904 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 17623085
TITLE: Phosphodiesterase 5 inhibitors lower both portal and pulmonary pressure in portopulmonary hypertension: a case report.
AUTHOR: Bremer Hinrich C; Kreisel Wolfgang; Roecker Kai; Dreher Michael; Koenig Daniel; Kurz-Schmieg Anna Katharina; Blum Hubert E; Roessle Martin; Deibert Peter
CORPORATE SOURCE: Department of Gastroenterology, Hepatology, Endocrinology and Infectious Diseases, University Hospital, Freiburg, Germany.. wolfgang.kreisel@uniklinik-freiburg.de
SOURCE: Journal of medical case reports, (2007) Vol. 1, pp. 46. Electronic Publication: 2007-07-10.
Journal code: 101293382. E-ISSN: 1752-1947.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED
ENTRY DATE: Entered STN: 8 Sep 2007
Last Updated on STN: 8 Dec 2007
AB ABSTRACT: BACKGROUND: Portopulmonary hypertension (PPHTN) is a severe complication in liver cirrhosis. PDE5 inhibitors lower pulmonary arterial pressure (PAP) in PPHTN. However, their effect on portal hypertension has not yet been investigated. CASE PRESENTATION: A 55 year

old male patient presented with PPHTN and alcoholic liver cirrhosis. 10 mg of Tadalafil, a PDE5 inhibitor with a long half-life, was administered orally under continuous monitoring of pulmonary and portal hemodynamics. For maintenance therapy the patient received Sildenafil 20 mg bid.Tadalafil lowered mean PAP from 45 to 39 mmHg within 60 minutes. Cardiac output (CO) increased from 6.8 to 7.9 l/min. Central venous pressure (CVP) remained stable at 3 mmHg. Systolic and diastolic blood pressure was lowered from 167/89 to 159/86 mmHg. Pulse rate increased from 75 to 87 per min. Wedged hepatic vein pressure (WHVP) decreased from 21 to 18 mm Hg, hepatovenous pressure gradient (HVPG) decreased from 10 to 7 mmHg. Hemodynamic monitoring after 6 months of Sildenafil therapy revealed a sustained lowering of mean PAP. HVPG remained constant at 10 mmHg. Cardiac and pulmonary performance had further improved. CONCLUSION: This case report shows for the first time, that phosphodiesterase 5 inhibitors lower both portal and pulmonary pressure in portopulmonary hypertension.

L1 ANSWER 3 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2007497047 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17715635
TITLE: Hepatopulmonary syndrome and portopulmonary hypertension: what's new?.
AUTHOR: Colle Isabelle; Van Steenkiste Christophe; Geerts Anja; Van Vlierberghe Hans
CORPORATE SOURCE: Department of Hepatology and Gastroenterology, Ghent University Hospital, Ghent, Belgium.. Isabelle.Colle@ugent.be
SOURCE: Acta gastro-enterologica Belgica, (2007 Apr-Jun) Vol. 70, No. 2, pp. 203-9. Ref: 67
Journal code: 0414075. ISSN: 0001-5644.
PUB. COUNTRY: Belgium
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200710
ENTRY DATE: Entered STN: 25 Aug 2007
Last Updated on STN: 12 Oct 2007
Entered Medline: 11 Oct 2007

AB Hepatopulmonary syndrome (HPS) is found in 4-47% of patients with cirrhosis and is characterized by intrapulmonary vascular dilatations especially in the basal parts of the lung. Liver injury and/or portal hypertension trigger the release of endothelin-1, TNF-alpha, cytokines and mediate vascular shear stress and release of nitric oxide and carbon monoxide, all contributing to intrapulmonary vasodilation. Severe HPS increases mortality (30%) after liver transplantation, especially if Pa O2 is below 50 mmHg. The diagnosis is made by calculating the alveolar-arterial oxygen gradient and by performing a contrast echocardiography. Medical therapy fails and the only long-term treatment available is liver transplantation. More than 85% experience significant improvement or complete resolution in hypoxaemia, but this may take more than 1 year. Portopulmonary hypertension (PPHT) occurs in 2-8% of the patients with cirrhosis. Imbalance between vasodilating (decreased pulmonary expression of eNOS and prostacyclin I2) and vasoconstrictive agents (increased expression of ET-1 and angiotensin 1) may be responsible for misguided angiogenesis and pulmonary hypertension. The diagnosis is made by performing an echocardiography and a right heart catheterisation when systolic pulmonary artery pressure is higher than 30 mmHg on echocardiography. Although prostacyclin analogues are efficacious, adverse effects in terms of safety, tolerability and drug delivery occur. Bosentan is probably the therapy of choice for patients with PPHT because it decreases pulmonary but can also diminish portal hypertension.

Sildenafil, a phosphodiesterase-5 inhibitor is used for idiopathic pulmonary hypertension, however, it should be used cautiously in patients with portal hypertension as it may increase portal hypertension by splanchnic vasodilation.

L1 ANSWER 4 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2007275338 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 17484815
TITLE: Hepatopulmonary syndrome and portopulmonary hypertension.
AUTHOR: Hendrickse Adrian; Azam Fareed; Mandell M Susan
CORPORATE SOURCE: Department of Anesthesiology, University of Colorado Health Sciences Center, 4200 East Ninth Avenue, Denver, CO 80262, USA.. susan.mandell@uchsc.edu
SOURCE: Current treatment options in cardiovascular medicine, (2007 Apr) Vol. 9, No. 2, pp. 127-36.
Journal code: 9815942. ISSN: 1092-8464.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED
ENTRY DATE: Entered STN: 9 May 2007
Last Updated on STN: 8 Dec 2007
AB The incidence of pulmonary vascular disorders is significantly increased in patients with liver disease. Intrapulmonary shunting with hypoxemia in patients with liver disease is diagnosed as hepatopulmonary syndrome (HPS), whereas precapillary pulmonary vessel obliteration is identified as portopulmonary hypertension (PPHTN). Because the symptoms of liver disease can mimic those of pulmonary vascular disease, all patients with hepatic failure should be screened for these two diseases. Pulse oximetry effectively screens for hypoxemia associated with HPS, whereas an elevated right ventricular systolic pressure estimated by echocardiography identifies patients at risk of having PPHTN. Liver transplantation is the only effective medical therapy for HPS. However, those who have a resting arterial oxygenation less than 50 mm Hg or a shunt measured by scintigraphic perfusion greater than 20% have an unacceptably high mortality rate following surgery. Compared with HPS, there are more therapeutic options that can bridge patients with PPHTN to transplantation. Drugs used to manage idiopathic pulmonary hypertension have shown promise in the treatment of PPHTN. Prostanoids, endothelin receptor antagonists, and phosphodiesterase-5 inhibitors have improved transplant survival. Despite treatment, however, perioperative mortality for patients with PPHTN remains high. Even with successful transplantation, HPS and PPHTN can persist or develop de novo. Long-term follow-up and surveillance of liver transplant recipients is thus indicated to identify HPS and PPHTN following surgery.

L1 ANSWER 5 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2007001493 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17197488
TITLE: PDE-5 inhibitors lower portal and pulmonary pressure in portopulmonary hypertension.
AUTHOR: Deibert P; Bremer H; Roessle M; Kurz-Schmieg A-K; Kreisel W
SOURCE: The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology, (2007 Jan) Vol. 29, No. 1, pp. 220-1.
Journal code: 8803460. ISSN: 0903-1936.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (CASE REPORTS)
Commentary
Letter

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200703
ENTRY DATE: Entered STN: 4 Jan 2007
Last Updated on STN: 24 Mar 2007
Entered Medline: 20 Mar 2007

L1 ANSWER 6 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2006614048 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17048047
TITLE: Portopulmonary hypertension.
AUTHOR: Halank Michael; Ewert Ralf; Seyfarth Hans-Juergen; Hoeffken Gert
CORPORATE SOURCE: Carl Gustav Carus University Dresden, Internal Medicine I, Fetscherstr. 74, 01307 Dresden, Germany.
SOURCE: Journal of gastroenterology, (2006 Sep) Vol. 41, No. 9, pp. 837-47. Ref: 86
Journal code: 9430794. ISSN: 0944-1174.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200701
ENTRY DATE: Entered STN: 19 Oct 2006
Last Updated on STN: 10 Jan 2007
Entered Medline: 9 Jan 2007
AB Portopulmonary hypertension (PPHT) is defined as precapillary pulmonary hypertension accompanied by hepatic disease or portal hypertension. Pulmonary hypertension results from excessive pulmonary vascular remodeling and vasoconstriction. These histological alterations have been indistinguishable from those of other forms of pulmonary arterial hypertension. Factors involved in the pathogenesis of PPHT include volume overload, hyperdynamic circulation, and circulating vasoactive mediators. The disorder has a substantial impact on survival and requires focused treatment. Liver transplantation in patients with moderate to severe PPHT is associated with a significantly reduced survival rate. The best medical treatment for patients with PPHT is controversial; most authors currently regard continuous intravenous application of prostacyclin as the treatment of choice for patients with severe PPHT. There is only very limited reported experience with inhaled prostacyclin or its analog, iloprost. Increasing evidence of the efficacy of the endothelin-receptor antagonist bosentan and of the phosphodiesterase-5 inhibitor sildenafil is emerging in highly selected patients with PPHT. In the future, a combination therapy of the above-mentioned agents might become a therapeutic option. Other agents such as beta-blockers seem to be harmful to patients with moderate to severe portopulmonary hypertension. Up-to-date, randomized, double-blind, controlled clinical trials are lacking and are needed urgently.

L1 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:304321 CAPLUS
DOCUMENT NUMBER: 149:347097
TITLE: Significant improvement of portopulmonary hypertension after 1-week terlipressin treatment
AUTHOR(S): Kalambokis, Georgios; Korantzopoulos, Panagiotis; Nikas, Spyros A.; Theodorou, Areti; Tsianos, Epameinondas V.
CORPORATE SOURCE: 1st Division of Internal Medicine, Medical School, University of Ioannina, Ioannina, 45110, Greece
SOURCE: Journal of Hepatology (2008), 48(4), 678-680

CODEN: JOHEEC; ISSN: 0168-8278
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cirrhosis associated with moderate and severe portopulmonary hypertension carries a poor prognosis. Optimal management has not yet been defined. Current treatment options, such as prostacyclin analogs, endothelin antagonists, and phosphodiesterase-5 inhibitors, are characterized by slow onset of action and various adverse effects, particularly in patients with advanced cirrhosis. Here, we report the significant reduction of pulmonary arterial pressure after 1-wk terlipressin treatment in a patient with concomitant hepato-renal syndrome. Terlipressin could be a novel and safe treatment for portopulmonary hypertension.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1066766 CAPLUS
DOCUMENT NUMBER: 145:389445
TITLE: Use of 2-phenyl-substituted imidazotriazinone derivative phosphodiesterase 5 inhibitors for the treatment of diseases treatable by increase of GMP levels
INVENTOR(S): Haning, Helmut; Serno, Peter; Bischoff, Erwin; Ulbrich, Ernst
PATENT ASSIGNEE(S): Bayer Healthcare A.-G., Germany
SOURCE: Ger. Offen., 27pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102005016345	A1	20061012	DE 2005-102005016345	20050409
CA 2603935	A1	20061019	CA 2006-2603935	20060327
WO 2006108506	A1	20061019	WO 2006-EP2774	20060327
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1871378	A1	20080102	EP 2006-723751	20060327
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008534634	T	20080828	JP 2008-504656	20060327

PRIORITY APPLN. INFO.: DE 2005-102005016345A 20050409
WO 2006-EP2774 W 20060327
OTHER SOURCE(S): MARPAT 145:389445
AB The invention discloses the use of phosphodiesterase 5 inhibitors generally, and in particular known 2-phenyl-substituted imidazotriazinone derivs., for the production of medicaments for the treatment of diseases treatable by increase of GMP levels in certain tissues, e.g.

pulmonary hypertension conditions, COPD, emphysema, chronic bronchial asthma, heart failure, etc. The invention also discloses combinations of these compds. with other therapeutic agents.

L1 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1303561 CAPLUS
DOCUMENT NUMBER: 144:285886
TITLE: Bosentan for the treatment of pulmonary arterial hypertension. (II)
AUTHOR(S): Antoniu, Sabina A.
CORPORATE SOURCE: Clinic of Pulmonary Disease, University of Medicine and Pharmacy, Iasi, 700070, Rom.
SOURCE: Therapy (2005), 2(6), 849-852
CODEN: THERCR; ISSN: 1475-0708
PUBLISHER: Future Drugs Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Portopulmonary hypertension is defined as pulmonary arterial hypertension occurring in the presence of portal hypertension. It is classified as a subset of pulmonary arterial hypertension and accordingly it is defined hemodynamically. Portopulmonary hypertension shares the main pathol. features as well as diagnostic approach with other forms of pulmonary arterial hypertension. Several nonpharmacol. and pharmacol. approaches are currently available. Among the pharmacol. approaches prostacycline and its derivs., phosphodiesterase-5 inhibitors such as sildenafil and endothelin receptor antagonists such as bosentan, have been used in portopulmonary hypertension treatment. This is a case series report on the long-term efficacy of bosentan treatment for severe (New York Heart Association functional Class III and IV) portopulmonary hypertension.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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NEWS 6 APR 26 USPATFULL and USPAT2 enhanced with patent assignment/reassignment information
NEWS 7 APR 28 CAS patent authority coverage expanded
NEWS 8 APR 28 ENCOMPLIT/ENCOMPLIT2 search fields enhanced
NEWS 9 APR 28 Limits doubled for structure searching in CAS

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                  introduction of free HIT display format
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 NEWS 15  MAY 28  CAS databases on STN enhanced with NANO super role in
                  records back to 1992
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=> s (phosphodiesterase or pde) and portal and (pressure or hypertens?)
L1          138 (PHOSPHODIESTERASE OR PDE) AND PORTAL AND (PRESSURE OR HYPERTENS
                ?)

=> s l1 and py<=2003
L2           28 L1 AND PY<=2003

=> dup rem l2
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PROCESSING COMPLETED FOR L2
L3 18 DUP REM L2 (10 DUPLICATES REMOVED)

=> d l3 ibib abs 1-18

L3 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:590998 CAPLUS
DOCUMENT NUMBER: 139:128037
TITLE: Use of acetylcholine esterase antagonists to treat insulin resistance
INVENTOR(S): Lautt, Wayne W.
PATENT ASSIGNEE(S): Diamedica Inc., Can.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061648	A1	20030731	WO 2003-CA78	20030127 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20030235609	A1	20031225	US 2003-350478	20030124 <--
CA 2514088	A1	20030731	CA 2003-2514088	20030127 <--
EP 1471905	A1	20041103	EP 2003-700275	20030127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005519906	T	20050707	JP 2003-561592	20030127
AU 2003201578	B2	20080306	AU 2003-201578	20030127
US 20050049293	A1	20050303	US 2004-502066	20041027
PRIORITY APPLN. INFO.:			US 2002-350958P P	20020125
			WO 2003-CA78 W	20030127

AB A method is provided for reducing insulin resistance in a mammalian subject, comprising administering a suitable acetylcholine esterase antagonist.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 18 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004050282 EMBASE
TITLE: Niemann-Pick disease: Sixteen-year follow-up of allogeneic bone marrow transplantation in a type B variant.
AUTHOR: Victor, S.; Coulter, J.B.S. (correspondence); Ellis, I.
CORPORATE SOURCE: Royal Liverpool Children's NHS Trust, Eaton Road, Liverpool L12 2AP, United Kingdom. j.coulter@rlch-tr.nwest.nhs.uk
AUTHOR: Besley, G.T.N.
CORPORATE SOURCE: Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, Manchester, United Kingdom.
AUTHOR: Desnick, R.J.; Schuchman, E.H.
CORPORATE SOURCE: Department of Human Genetics, Mount Sinai Sch. of Med. of NY Univ., New York, NY, United States.

AUTHOR: Vellodi, A.
CORPORATE SOURCE: Great Ormond Street Hospital, Children NHS Trust, London, United Kingdom.
SOURCE: Journal of Inherited Metabolic Disease, (2003) Vol. 26, No. 8, pp. 775-785.
Refs: 28
ISSN: 0141-8955 CODEN: JIMDDP
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
026 Immunology, Serology and Transplantation
029 Clinical and Experimental Biochemistry
048 Gastroenterology
007 Pediatrics and Pediatric Surgery
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Feb 2004
Last Updated on STN: 12 Feb 2004

AB Allogenic bone marrow transplantation (BMT) was carried out on a 3-year-old white caucasian girl with Niemann-Pick disease (NPD) type B. The donor was her unaffected brother. The patient was neurologically normal at the time of transplantation. Engraftment was based on cytogenetic studies and increased leukocyte acid sphingomyelinase (ASM) activity. However, liver biopsies taken up to 33 months post transplantation showed only a moderate reduction in stored sphingomyelin and no significant increase in ASM activity. The post-transplantation period was complicated by severe graft-versus-host disease and a respiratory arrest. By 6 years of age, neurological involvement was observed, including bilateral cherry red spots. The proband is now severely mentally and physically disabled. Liver cirrhosis has continued to progress despite the BMT, and haematemesis due to portal hypertension occurred at 17 years of age. However, pulmonary infiltration regressed after BMT and there has been no clinical evidence of pulmonary insufficiency.

L3 ANSWER 3 OF 18 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
DUPLICATE 1
ACCESSION NUMBER: 2003:179159 BIOSIS
DOCUMENT NUMBER: PREV200300179159
TITLE: Portopulmonary hypertension: A tale of two circulations.
AUTHOR(S): Budhiraja, Rohit; Hassoun, Paul M. [Reprint Author]
CORPORATE SOURCE: Division of Pulmonary and Critical Care, Johns Hopkins University School of Medicine, 5501 Hopkins Bayview Circle, Baltimore, MD, 21224, USA
SOURCE: Chest, (February 2003) Vol. 123, No. 2, pp. 562-576. print.
ISSN: 0012-3692 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Apr 2003
Last Updated on STN: 9 Apr 2003

AB Pulmonary involvement is common in patients with portal hypertension and can manifest in diverse manners. Changes in pulmonary arterial resistance, manifesting either as the hepatopulmonary syndrome or portopulmonary hypertension (PPHTN), have been increasingly recognized in these patients in recent years. This review summarizes the clinicopathologic features, diagnostic criteria, as well as the latest concepts in the pathogenesis and management of PPHTN, which is defined as an elevated pulmonary artery pressure in the setting

of an increased pulmonary vascular resistance and a normal wedge pressure in a patient with portal hypertension
.

L3 ANSWER 4 OF 18 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003179790 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12644956
TITLE: Pulmonary hypertension.
AUTHOR: Nicod Laurent P
CORPORATE SOURCE: Pulmonary division, University Hospital, Geneva, Switzerland.. laurent.nicod@hcuge.ch
SOURCE: Swiss medical weekly : official journal of the Swiss Society of Infectious Diseases, the Swiss Society of Internal Medicine, the Swiss Society of Pneumology, (2003 Feb 22) Vol. 133, No. 7-8, pp. 103-10. Ref: 52
Journal code: 100970884. ISSN: 1424-7860.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 18 Apr 2003
Last Updated on STN: 28 Jun 2003
Entered Medline: 27 Jun 2003
AB Pulmonary arterial hypertension (PAH) must be classified into primary pulmonary hypertension and PAH related to other diseases such as collagen vascular diseases, HIV infection or portal hypertension. PAH must also be differentiated from other entities, in particular pulmonary hypertension secondary to thromboembolic diseases, requiring specific approaches. All PAH results in similar histological remodelling of pulmonary arteries, with thickening of the intima, proliferation of the media and plexogenic lesions. Today the physiopathology of these lesions is much better understood and has resulted in new therapies involving substances such as prostacyclins, endothelin receptor antagonists or phosphodiesterase inhibitors, aimed not only at dilating arteries but also at preventing their remodelling. Thromboendarterectomy, septostomy and transplantation remain the only option where medical treatment has failed.

L3 ANSWER 5 OF 18 EMBASE
ACCESSION NUMBER: 2003037205 EMBASE
TITLE: Nitric oxide in liver transplantation: Pathobiology and clinical implications.
AUTHOR: Shah, Vijay, Dr. (correspondence); Kamath, Patrick S.
CORPORATE SOURCE: GI Research Unit, Advanced Liver Disease Study Group, Department of Medicine, 200 First St. SW, Rochester, MN 55905, United States. shah.vijay@mayo.edu
AUTHOR: Shah, Vijay, Dr. (correspondence)
CORPORATE SOURCE: GI Research Unit, Mayo Clinic, Advanced Liver Disease Study Group, 200 First St. SW, Rochester, MN 55905, United States. shah.vijay@mayo.edu
SOURCE: Liver Transplantation, (1 Jan 2003) Vol. 9, No. 1, pp. 1-11.
Refs: 114
ISSN: 1527-6465 CODEN: LITRFO
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology

037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 2003
Last Updated on STN: 30 Jan 2003
AB The gaseous molecule nitric oxide is involved in a variety of liver transplant-relevant processes, including ischemia-reperfusion injury, acute cellular rejection, and circulatory changes characteristic of advanced liver disease. This review article focuses on new advances relating to the role of nitric oxide in these syndromes with an emphasis on pathobiology and potential clinical implications.

L3 ANSWER 6 OF 18 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:583292 BIOSIS
DOCUMENT NUMBER: PREV200300573100
TITLE: SILDENAFIL IN RATS WITH CIRRHOSIS AND PORTAL HYPERTENSION: SYSTEMIC AND SPLANCHNIC HAEMODYNAMIC EFFECTS.
AUTHOR(S): Colle, Isabelle [Reprint Author]; De Vriese, An; Van Vlierberghe, Hans; Lameire, Norbert; De Vos, Martine
CORPORATE SOURCE: Gent, Belgium
SOURCE: Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. S1553. e-file. Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003
AB OBJECTIVES: Sildenafil is a selective inhibitor of the cGMP-specific phosphodiesterase type V (PDE-V) in the corpus cavernosum. PDE-V is also present in the mesenteric artery. Cirrhosis is complicated by a splanchnic vasodilation attributed to a local overproduction of nitric oxide (NO). As sildenafil potentiates the effects of NO, it may further decrease mesenteric vascular tone and increase portal venous blood flow. The aim is to evaluate the effects of sildenafil on the systemic and splanchnic haemodynamics in an experimental model of cirrhosis. METHODS: Secondary biliary cirrhosis was induced in male Wistar rats by common bile duct ligation (CBDL, n = 8); control rats were sham-operated (sham, n = 7). Mean arterial pressure (MAP), portal venous pressure (PVP) and arterial mesenteric blood flow (MBF) were measured after intramesenteric (i.m.) (0.01 to 10 mg/kg) and after intravenous (i.v.) (0.01 to 10 mg/kg) administration of sildenafil. RESULTS: Baseline PVP was significantly higher in CBDL than in sham rats, whereas baseline MAP tended to be lower and MBF tended to be higher in CBDL compared with sham rats. Both i.m. and i.v. injection of sildenafil significantly decreased MAP and increased MBF and PVP in a dose-dependent way. The decrease in MAP was significantly lower in CBDL than in sham rats. The increase in MBF was significantly lower in CBDL than in sham rats. PVP tended to increase more importantly in sham rats than in CBDL. CONCLUSION: Sildenafil increases MBF and PVP and induces systemic hypotension. The effects are less pronounced in cirrhosis, suggesting vascular hyporesponsiveness to sildenafil. Although the rise in PVP in cirrhotic animals is smaller than in controls, it may present a risk for hemorrhagic complications. Further studies are necessary before prescribing

sildenafil to patients with cirrhosis..

L3 ANSWER 7 OF 18 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002440718 EMBASE
TITLE: Pulmonary hypertension in the young.
AUTHOR: Haworth, Sheila G., Prof. (correspondence)
CORPORATE SOURCE: Institute of Child Health, 30 Guilford Street, London WC1N 1EH, United Kingdom. S.Haworth@ich.ucl.ac.uk
SOURCE: Heart, (Dec 2002) Vol. 88, No. 6, pp. 658-664.
Refs: 21
ISSN: 1355-6037 CODEN: HEARFR
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
007 Pediatrics and Pediatric Surgery
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Dec 2002
Last Updated on STN: 19 Dec 2002

L3 ANSWER 8 OF 18 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:626747 BIOSIS
DOCUMENT NUMBER: PREV200200626747
TITLE: Systemic and splanchnic hemodynamic effects of sildenafil in rats with cirrhosis and portal hypertension.
AUTHOR(S): Colle, Isabelle [Reprint author]; De Vriese, An [Reprint author]; Van Vlierberghe, Hans [Reprint author]; Lameire, Norbert [Reprint author]; De Vos, Martine [Reprint author]
CORPORATE SOURCE: University Hospital Ghent, Ghent, Belgium
SOURCE: Hepatology, (October, 2002) Vol. 36, No. 4 Part 2, pp. 510A. print.
Meeting Info.: 53rd Annual Meeting on the Liver. BOSTON, MA, USA. November 01-05, 2002.
CODEN: HPTLD9. ISSN: 0270-9139.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 2002
Last Updated on STN: 12 Dec 2002

L3 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:257685 CAPLUS
DOCUMENT NUMBER: 128:289810
ORIGINAL REFERENCE NO.: 128:57231a,57234a
TITLE: Hemodynamics and oxygen metabolism in a canine model where sepsis was induced by fecal peritonitis
AUTHOR(S): Tanaka, Yoshikazu
CORPORATE SOURCE: Second Department of Anesthesiology, Dokkyo University School of Medicine, Tochigi, 321-0293, Japan
SOURCE: Dokkyo Igakkai Zasshi (1998), 13(1), 185-199
CODEN: DIZAEG; ISSN: 0911-5900
PUBLISHER: Dokkyo Igakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The objective of this study was to clarify hemodynamics and oxygen metabolism in an canine model where sepsis was induced by fecal peritonitis, and to examine the pharmacol. actions of beta-adrenergic stimulant, dobutamine, and phosphodiesterase III inhibitor, amrinone, as a therapeutic

agent. Twenty mongrel dogs were anesthetized with pentobarbital and ventilated mech. Fecal peritonitis was induced by instilling 1.0 g/kg BW of the fecal mixture for 5 h. Plasma endotoxin was detected 3 h after instillation. Peritonitis caused decreases in mean arterial pressure, cardiac output, superior mesenteric arterial and portal venous blood flow, systemic oxygen delivery, and arterial and mixed venous oxygen saturation Systemic oxygen consumption was elevated significantly. Microscopical evaluation revealed epithelial lifting at the tip of the villus. Treatment with dobutamine infusion (5μg/kg/min) at 3 h after fecal peritonitis improved the intestinal blood flow and oxygen extraction ratio, and prevented the development of intestinal blood flow and oxygen extraction ratio, and prevented the development of intestinal mucosal damage. On the other hands, amrinone (10μg/kg/min) decreased mean arterial pressure, increased oxygen consumption and oxygen extraction ratio, and did not prevent mucosal damage. It was concluded that endotoxemia was developed 3 h after fecal peritonitis. Potential application of dobutamine, but not amrinone, may exist in treatment of septic patient.

L3 ANSWER 10 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1998088826 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9428550
TITLE: Pentoxifylline increases gut ketogenesis following trauma and hemorrhagic shock.
AUTHOR: Wang W; Wang P; Chaudry I H
CORPORATE SOURCE: Center for Surgical Research, Department of Surgery, Brown University School of Medicine and Rhode Island Hospital, Providence 02903, USA.
CONTRACT NUMBER: KO2 AI 01461 (United States NIAID NIH HHS)
R01 GM 39519 (United States NIGMS NIH HHS)
SOURCE: Critical care medicine, (1998 Jan) Vol. 26, No. 1, pp. 101-7.
Journal code: 0355501. ISSN: 0090-3493.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 6 Feb 1998
Last Updated on STN: 29 Jan 1999
Entered Medline: 28 Jan 1998

AB OBJECTIVES: Although pentoxifylline produces various beneficial effects following adverse circulatory conditions, it is not known whether this agent has any effects on gut lipid metabolism after trauma-hemorrhage and resuscitation. The aim of this study, therefore, was to determine whether or not administration of pentoxifylline after trauma-hemorrhagic shock has any salutary effects on gut ketogenesis. DESIGN: A prospective, controlled animal study. SETTING: A university research laboratory. SUBJECTS: Fifty-six male Sprague-Dawley rats. INTERVENTIONS: Rats underwent a midline laparotomy (i.e., trauma-induced) and were bled to and maintained at a mean arterial pressure of 40 mm Hg until 40% of the shed blood volume was returned in the form of lactated Ringer's solution. The animals were then resuscitated with four times the volume of maximal bleedout with lactated Ringer's solution over 60 mins. Pentoxifylline (50 mg/kg body weight) or an equivalent volume of normal saline was infused intravenously over 100 mins during and after resuscitation. For in vivo lipid loading, one milliliter of olive oil was given intraduodenally on the completion of resuscitation. Blood samples from portal vein and carotid artery, as well as enterocytes from proximal small intestine, were obtained at 1.5 hrs after fat feeding.

MEASUREMENTS AND MAIN RESULTS: Mitochondrial fatty acid beta-oxidation enzyme (i.e., palmitoyl-coenzyme A dehydrogenase) activity, as well as portal and arterial plasma beta-hydroxybutyrate values, were determined. Palmitoyl-coenzyme A dehydrogenase activity in villus tip cells and plasma beta-hydroxybutyrate values in portal vein and carotid artery were significantly reduced after trauma-hemorrhage and resuscitation. Pentoxifylline administration, however, significantly increased mitochondrial fatty acid beta-oxidation enzyme activity and portal plasma beta-hydroxybutyrate concentration without significantly affecting arterial concentrations under such conditions. CONCLUSION: Pentoxifylline promotes gut ketogenesis following trauma-hemorrhage and resuscitation.

L3 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1998:476921 CAPLUS
DOCUMENT NUMBER: 129:254660
ORIGINAL REFERENCE NO.: 129:51695a,51698a
TITLE: Acute effects of toborinone on vascular capacitance and conductance in experimental heart failure
AUTHOR(S): Semeniuk, Lisa M.; Belenkie, Israel; Tyberg, John V.
CORPORATE SOURCE: Departments of Medicine and Physiology and Biophysics, The University of Calgary, Calgary, AB, T2N 4N1, Can.
SOURCE: Circulation (1998), 98(1), 58-63
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Toborinone (OPC-18790), a phosphodiesterase III inhibitor, enhances cardiac contractility and is an arterial dilator. However, its effects on the venous system have not yet been clearly defined. Because toborinone administration reduces left ventricular (LV) end-diastolic pressure, it is probably also a venodilator. Because of the known arterial effects and the hypothesized venous effects, we compared changes in systemic vascular conductance (the inverse of resistance) with changes in venous capacitance. In 15 anesthetized, splenectomized dogs (10 treatment, 5 control), pressures were measured in the right atrium, aorta, portal vein, and LV. A cuff constrictor was placed around the portal vein. Cardiac output was measured by thermodilution, and splanchnic vascular capacitance was measured by blood-pool scintigraphic methods. Data were collected at baseline, after induction of heart failure (microsphere embolization into the left coronary artery), and then after toborinone boluses of 0.1, 0.2, 0.4, and 0.8 mg/kg. Heart failure was associated with decreased capacitance and conductance (to 87±3% and 64±4% of baseline values, resp., $P<0.05$). After administration of the lower doses of toborinone, capacitance increased more than conductance; however, the effects were more balanced at the higher doses. Compared with nitroglycerin, hydralazine, and enalaprilat (results of an earlier study) in the same model, toborinone increased capacitance to a degree similar to that with nitroglycerin, at higher doses increased conductance similarly to hydralazine, and increased both capacitance and conductance considerably more than did enalaprilat. Toborinone is a potent balanced venous and arterial dilator in exptl. acute heart failure. These marked effects suggest that it may prove to be a clin. important alternative to other vasodilators.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 18 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1997074839 EMBASE
TITLE: Heterogeneity of liver disorder in type B Niemann-Pick disease.

AUTHOR: Takahashi, Tsutomu, Dr. (correspondence)
CORPORATE SOURCE: Department of Pediatrics, Akita University School of Medicine, 1-1-1 Hondo, Akita-shi, Akita 010, Japan.
AUTHOR: Akiyama, Kenji; Tomihara, Masako; Tokudome, Takahiro; Nishinomiya, Fujihiko; Tazawa, Yusaku; Horinouchi, Kenichi; Sakiyama, Takeshi; Takada, Goro
SOURCE: Human Pathology, (1997) Vol. 28, No. 3, pp. 385-388.
Refs: 12
ISSN: 0046-8177 CODEN: HPCQA4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Mar 1997
Last Updated on STN: 24 Mar 1997

AB Patients with type B Niemann-Pick disease (NPD) are known to be complicated with varying degrees of prognosis-determining liver dysfunction. To see heterogeneity of the dysfunction histologically, we performed liver biopsies on three NPD patients from three different families, who were diagnosed by enzyme assay of acid sphingomyelinase (ASM) and analysis of the ASM gene. In a severe case, of a female patient in her childhood, the liver showed definite fibrosis despite her age. In contrast, in a very mild case, of an adult male patient, the liver showed little fibrosis, though the ballooning of hepatocytes and infiltration of foamy histiocytes were observed in the tissue. Three homo-allelic mutations (S436R, A599T, and S231P) were identified in the patients. Thus, various hepatic phenotypes in type B NPD were shown to be caused by the heterogeneity of liver lesions originating from different ASM gene mutations.

L3 ANSWER 13 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1998201168 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9540345
TITLE: Effect of amrinone on portal hemodynamics and tissue blood flow in the isolated perfused rat liver.
AUTHOR: Kariya N
CORPORATE SOURCE: Department of Anesthesiology and Intensive Care Medicine, Osaka City University Medical School, Japan.
SOURCE: Osaka city medical journal, (1997 Dec) Vol. 43, No. 2, pp. 243-51.
Journal code: 0376413. ISSN: 0030-6096.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 7 May 1998
Last Updated on STN: 7 May 1998
Entered Medline: 30 Apr 1998

AB We studied the effect of amrinone on portal perfusion pressure, perfusion flow, and tissue blood flow using an isolated perfused rat liver model. In the constant perfusion flow model, amrinone effectively decreased perfusion pressure in the precontracted state by adenosine triphosphate (ATP) or norepinephrine. Amrinone dose-dependently decreased portal perfusion pressure increased by calcium chloride. Similarly, amrinone dose-dependently increased portal perfusion flow decreased by ATP in the constant perfusion pressure model. Amrinone effectively increased tissue blood flow decreased by ATP or norepinephrine measured by laser-Doppler flowmetry. A specific inhibitor of the biosynthesis of nitric oxide, N

omega-nitro-L-arginine, did not affect the hemodynamic effect of amrinone, suggesting that nitric oxide is not involved in the portal vasodilating effect of amrinone. We conclude that amrinone increases portal blood flow by decreasing perfusion pressure and contributes to increasing tissue blood flow of the liver without the involvement of nitric oxide.

L3 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1995:396408 CAPLUS
DOCUMENT NUMBER: 122:157633
ORIGINAL REFERENCE NO.: 122:29029a,29032a
TITLE: Change in vascular cAMP and cGMP contents in portal hypertensive rats
AUTHOR(S): Huang, Yi-Tsau; Lo, Jeng-Wu; Lin, Han-Chieh; Tsai, Yang-Te; Hong, Chaung-Ye; Yang, May C. M.
CORPORATE SOURCE: Institute Traditional Medicine, National Yang Ming Medical College, Taipei, Taiwan
SOURCE: Pharmacology (1995), 50(2), 86-91
CODEN: PHMGBN; ISSN: 0031-7012
PUBLISHER: Karger
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to investigate the possible changes of cyclic nucleotide contents in portal hypertensive rats. Portal hypertension was induced by partial portal vein ligation (PVL) in Sprague-Dawley rats. Sham-operated rats served as controls. Hemodynamic and cyclic nucleotide measurements were performed at 14 days after surgery. The portal venous pressure was significantly higher, while systemic arterial pressure and heart rate were lower in PVL rats than those in controls. Basal cAMP (PVL, 10.91 ± 0.98, vs. sham, 8.08 ± 0.81 pmol/mg protein) and cGMP (PVL, 0.91 ± 0.12, vs. sham, 0.59 ± 0.05 pmol/mg protein) contents in the tail artery were significantly higher in PVL rats. Isobutyryl methylxanthine (10-5 M), a nonspecific phosphodiesterase inhibitor, exerted similarly stimulating effects on the tissue cAMP (PVL, 158 ± 10, vs. sham, 178 ± 20%) and cGMP (295 ± 28 vs. 316 ± 71%) levels in both PVL and control rats; so did forskolin (10-6 M) on the cAMP (184 ± 20 vs. 197 ± 66%) content in both groups. Our results showed that the arterial cAMP and cGMP contents were higher in PVL rats, which may contribute to the reduction of peripheral resistance in portal hypertension.

L3 ANSWER 15 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1987017279 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3763677
TITLE: The effects of PAF-acether on the cardiovascular system and their inhibition by a new highly specific PAF-acether receptor antagonist BN 52021.
AUTHOR: Baranes J; Hellegouarch A; Le Hegarat M; Viossat I; Auguet M; Chabrier P E; Braquet P
SOURCE: Pharmacological research communications, (1986 Aug) Vol. 18, No. 8, pp. 717-37.
Journal code: 0236354. ISSN: 0031-6989.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198611
ENTRY DATE: Entered STN: 2 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 19 Nov 1986

AB BN 52021, a new specific PAF-acether receptor antagonist, was evaluated on several cardiovascular models. BN 52021 antagonized PAF-acether-induced extravasation in rats. Inhibition of the hypotensive action of PAF-acether was obtained by administration of the antagonist, given preventively or curatively. In isolated guinea-pig hearts, BN 52021 inhibited the vasoconstriction induced by PAF-acether whereas a small inhibition was observed with papaverine. On the other hand, phosphodiesterase inhibitors were very effective against coronary vasoconstriction induced by vasopressin while BN 52021 was without effect. PAF-acether increased the tonus of rat isolated portal vein; this effect was inhibited by BN 52021, without any reduction in basal myogenic activity. In this model Ca2+ antagonists (D 600, diltiazem) showed a small inhibitory effect but they strongly reduced basal myogenic activity. Neither PAF-acether nor BN 52021 modified phenylephrine-induced contraction of the isolated rabbit aorta with or without endothelium demonstrating that endothelium-dependent relaxing factor is not related to PAF-acether. Our results suggest that BN 52021 specifically block the cardiovascular effects of PAF-acether. This agent may thus be an useful tool for a better understanding of the role of PAF-acether in hemodynamic changes involved in anaphylaxis or shock.

L3 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1984:32896 CAPLUS
DOCUMENT NUMBER: 100:32896
ORIGINAL REFERENCE NO.: 100:5091a,5094a
TITLE: Effects of sodium-decreased media on tonus and of spasmolytics on the responses to contractile agents in portal veins from SHRSP and WKY [rats]
AUTHOR(S): Murakami, Noriko; Niwa, Atsuko; Higashino, Hideaki; Suzuki, Aritomo
CORPORATE SOURCE: Sch. Med., Kinki Univ., Osaka, 659, Japan
SOURCE: Vasc. Neuroeff. Mech., Int. Symp., 4th (1983), Meeting Date 1981, 413-16. Editor(s): Bevan, John A. Raven: New York, N. Y.
CODEN: 50PUAW
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Isometric contractions of portal vein sections from stroke-prone spontaneously hypertensive rats (SHRSP) (induced by acetylcholine, norepinephrine, KCl, or BaCl2) were inhibited by dibutyryl cAMP, aminophylline (a phosphodiesterase inhibitor), or fenoterol (a β-stimulant) less than the vein sections from normal control Wistar Kyoto rats (WKY). Diltiazem (a Ca antagonist) inhibited the contractions in SHRSP more than in control WKY rats. The replacement of normal incubation medium (Locke's solution) by medium with low Na and(or) Ca concns. caused stronger contractions in SHRSP than in WKY controls. Thus, in SHRSP portal veins, the reactivity to cAMP is decreased; the reactivity of β-receptors is impaired; and Ca transport into cells and/or Ca release from cell stores are accelerated as compared with those of WKY rats.

L3 ANSWER 17 OF 18 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1982:27102 BIOSIS
DOCUMENT NUMBER: PREV198222027102; BR22:27102
TITLE: EFFECTS OF SOME SPASMOLYTICS ON RESPONSES TO SMOOTH MUSCLE CONTRACTILE AGENTS EXPERIMENT IN THE ISOLATED PORTAL VEIN FROM STROKE PRONE SPONTANEOUSLY HYPERTENSIVE RATS.
AUTHOR(S): MURAKAMI N [Reprint author]; YANAGAWA T; HIGASHINO H; MIYAZATO A S T; NIWA A
CORPORATE SOURCE: DEP PHARMACOL, KINKI UNIV SCH MED, OSAKA-FU 589

SOURCE: Japanese Heart Journal, (1981) Vol. 22, No. 3, pp. 491.
Meeting Info.: 16TH ANNUAL SCIENTIFIC MEETING OF THE COUNCIL FOR THE SPONTANEOUSLY HYPERTENSIVE RAT (SHR), YAMAGATA, JAPAN, OCTOBER 1-2, 1980. JPN HEART J.
CODEN: JHEJAR. ISSN: 0021-4868.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH

L3 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 1975:84098 CAPLUS
DOCUMENT NUMBER: 82:84098
ORIGINAL REFERENCE NO.: 82:13468h,13469a
TITLE: Cyclic AMP [of] blood vessels of spontaneously hypertensive rat
AUTHOR(S): Ramanathan, S.; Shibata, Shoji
CORPORATE SOURCE: Sch. Med., Univ. Hawaii, Honolulu, HI, USA
SOURCE: Blood Vessels (1974), 11(5), 312-18
CODEN: BLVSAB; ISSN: 0303-6847
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The vascular smooth muscle (aorta, portal vein, and renal arteries) from spontaneously hypertensive rats (SHR) contained a lower level of cyclic AMP. Similar differences were observed in young SHR that had not yet developed hypertension, as compared to their normotensive controls. However, no such difference was observed in the vascular smooth muscle from the cross-bred normotensive animals. The adenyl cyclase and phosphodiesterase activities of the vascular smooth muscles from SHR was lower than the normotensive controls. Changes in cyclic AMP metabolism may occur during the process of hypertension .

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                  STN Easy
 NEWS 13  MAY 14  DGENE, PCTGEN and USGENE enhanced with increased
                  limits for exact sequence match searches and
                  introduction of free HIT display format
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L3   ANSWER 1 OF 2  EMBASE  COPYRIGHT (c) 2009 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:   2003098686  EMBASE
TITLE:              Portopulmonary hypertension: A tale of two
                    circulations.
AUTHOR:             Budhiraja, Rohit; Hassoun, Paul M., Dr. (correspondence)
CORPORATE SOURCE:   Department of Medicine, Tufts-New England Medical Center,
                    Tufts University School of Medicine, Boston, MA, United
                    States.
AUTHOR:             Hassoun, Paul M., Dr. (correspondence)
CORPORATE SOURCE:   Department of Medicine, Johns Hopkins Univ. Sch. of
                    Medicine, Div. of Pulmonary and Critical Care, 5501 Hopkins
                    Bayview Circle, Baltimore, MD 21224, United States.
SOURCE:             Chest, (1 Feb 2003) Vol. 123, No. 2, pp. 562-576.
                    Refs: 208
                    ISSN: 0012-3692  CODEN: CHETBF
COUNTRY:            United States
DOCUMENT TYPE:      Journal; General Review; (Review)
FILE SEGMENT:       015     Chest Diseases, Thoracic Surgery and Tuberculosis
                    037     Drug Literature Index
                    038     Adverse Reactions Titles
                    048     Gastroenterology
LANGUAGE:           English
SUMMARY LANGUAGE:   English
ENTRY DATE:         Entered STN: 25 Mar 2003
                    Last Updated on STN: 25 Mar 2003
AB   Pulmonary involvement is common in patients with portal hypertension and
     can manifest in diverse manners.  Changes in pulmonary arterial
     resistance, manifesting either as the hepatopulmonary syndrome or
     portopulmonary hypertension (PPHTN), have been increasingly
     recognized in these patients in recent years.  This review summarizes the
     clinicopathologic features, diagnostic criteria, as well as the latest
     concepts in the pathogenesis and management of PPHTN, which is defined as
     an elevated pulmonary artery pressure in the setting of an increased
     pulmonary vascular resistance and a normal wedge pressure in a patient
     with portal hypertension.

L3   ANSWER 2 OF 2  BIOSIS  COPYRIGHT (c) 2009 The Thomson Corporation  on STN
ACCESSION NUMBER:   2003:127784  BIOSIS
DOCUMENT NUMBER:    PREV200300127784
TITLE:              Acute and short-term hemodynamic and clinical effect of
                    sildenafil in pulmonary arterial hypertension.
AUTHOR(S):          McGoon, M. D. [Reprint Author]; Frantz, R. P. [Reprint
                    Author]; Severson, C. J. [Reprint Author]; Durst, L. A.
                    [Reprint Author]; Tointon, S. K. [Reprint Author]
CORPORATE SOURCE:   Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA
SOURCE:             Journal of Heart and Lung Transplantation, (January
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2003) Vol. 22, No. 1S, pp. S153. print.
Meeting Info.: Twenty-Third Annual Meeting and Scientific Sessions of the International Society for Heart and Lung Transplantation. Vienna, Austria. April 09-12, 2003. International Society for Heart and Lung Transplantation.
ISSN: 1053-2498.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 2003
Last Updated on STN: 5 Mar 2003

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